THE
JOURNAL OF MENTAL SCIENCE

*[Published by Authority of the
Royal Medico-Psychological Association]*

No. 443 [NEW SERIES NO. 407] APRIL, 1960 VOL. 106

Original Articles

THE FIRST COMMISSIONERS: REFORM IN SCOTLAND IN THE MID-NINETEENTH CENTURY

THE PRESIDENTIAL ADDRESS AT THE ONE HUNDRED AND NINETEENTH ANNUAL MEETING OF THE ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION HELD AT THE GLASGOW ROYAL MENTAL HOSPITAL, 15 JULY, 1959

By

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MY first duty is to thank you for the very great honour you have done me in electing me to the office of President of the Royal Medico-Psychological Association, an office which in the past has been held by so many distinguished men in comparison with whom I feel very unworthy. I am greatly touched by this evidence of your goodwill.

I am the second Superintendent of Gartnavel who, in his period of office, has been elected President. The first was Dr. David Yellowlees, who was President in 1890. His sons, Dr. David and Dr. Henry Yellowlees, who have both attained a very high place in our specialty, were born in this hospital. I have been closely associated with Dr. David Yellowlees, who was a pioneer in the practice of psychotherapy in Glasgow and in the West of Scotland and who until recently was the Director of the Lansdowne Clinic, a post which he filled with great distinction. I greatly value his friendship and I am glad that he is here today.

Another former Physician Superintendent of Gartnavel who is a Past President of the Association is Sir David Henderson, though at the time of his Presidency in 1946 he had long been Physician Superintendent at Morningside and Professor of Psychiatry at Edinburgh University.

Moreover, I have noted with great personal interest that at the Gartnavel meeting in 1890, the Gaskell Prize was presented to Sir David Henderson's predecessor at Edinburgh, Dr. George Robertson, who was later my own Chief at Morningside. He too became President of the Association some thirty years later.

At that meeting in 1890, Dr. Yellowlees chose as the topic for his address the view which was then strongly held and which he disagreed with and criticized, that the causes of mental illness were invariably the result of pathological changes in the body and particularly in the brain. Dr. Yellowlees put this view as follows: "In the pride of pathological research we speak of nothing but bodily conditions as the cause of mental disorders, and the mind is degraded to the level of a secretion, a little more respectable than bile because the brain is more complex than the liver, but a mere secretion after all and only what the brain makes it. The notion that mind can influence brain as truly as brain influences mind is laughed to scorn." This view had found expression in the report of a committee of the London County Council in which the treatment of patients in mental hospitals was criticized, and in which it was recommended that a special hospital should be established in London, in which the mentally disordered would be under the care of general hospital physicians and surgeons. Dr. Yellowlees devoted much of his address to a constructive criticism of this proposal.

I began my psychiatric career in this hospital in 1925, and to Sir David Henderson, who was then Superintendent and to others who have been my teachers, I owe a great debt of gratitude and I think it is perhaps proper that I should refer to them individually.

Dr. Edwin Goodall, to whom I was for a short time senior assistant at the Whitchurch Mental Hospital, Cardiff, tried without much success to teach me the value of method and order in hospital administration. He also tried, and in this I regret to say he was again unsuccessful, to interest me in biochemical research, to which he was himself devoted. He established at Whitchurch a well-equipped laboratory, and we all know the valuable research which has been carried out there, in which one of our distinguished Past Presidents, Dr. P. K. McCowan, has had so important a part.

That great and lovable man, Dr. Adolf Meyer, under whom I had the very great honour to serve for a short time, inspired me as he did everyone else with his immense knowledge, his breadth of vision and his high ideals.

To the late Professor George Robertson I owe an important step in my career, for he invited me to become his senior assistant at Morningside in 1927. During the five years I was with him, first as senior assistant and later as deputy, he gave me as much clinical and administrative independence as I think would have satisfied the most progressive modern consultant.

Professor Robertson was a man of restless and adventurous spirit. He would have been delighted with the present-day tendencies in mental health legislation, particularly the proposed non-designation of mental hospitals. Indeed, he anticipated this development in Morningside by instituting the treatment of patients in nursing homes, and by the foundation of the Jordanburn Nerve Hospital. The provision he made for the indoor and outdoor treatment of mental illness for all classes of the community, was a remarkable achievement. With its two mental hospitals, Craig House and West House, the Jordanburn Nerve Hospital with its out-patient department, the out-patient clinic at the Royal Infirmary, the associated child guidance clinic, and the hospital's Physician Superintendent holding the Chair of Psychiatry at Edinburgh University, the organization of Morningside was unique in its scope and possibilities for development. It was something which we shall never see again.

It is, however, to Sir David Henderson that I feel I owe most. I owe much to him for his teaching and for his encouragement. But above all I feel indebted to him for the example he set as a clinician in his regard for the patient as a human being, for whom it was one's duty to do certain things, but also a duty to refrain from doing certain things. It was this strict ethical standard founded on the principle of respect for the patient as an individual that impressed me as a young man, and it is this attitude of mind in Sir David, which has never changed or varied throughout the years, which to me even transcends his unsurpassed gifts as a clinician and as a teacher. I think he is a very great man and my respect and admiration for him have grown throughout the years.

I have chosen as the subject of my address, the contribution of the Board of Lunacy, or as it later became the Scottish Board of Control, in the development of the mental health services in Scotland. It is a subject about which many in the audience are already well informed and I cannot claim any originality in my treatment of it, and I fear that most of what I have to say is only "cauld kail het again".

Nevertheless, the recent report of the Royal Commission on the Lunacy Laws, and the changes which are about to be made in the law relating to mental illness in England and in Scotland, may serve as an excuse to look back on the situation as it was one hundred years ago and to compare the problems of today with those of yesterday. We may find that matters which concerned the mental specialists of that day were not unlike those that worry us today; and that the views then held on mental illness and mental hospitals are not completely outdated today.

I hope to convince you that not only did the Board of Lunacy in its early days do much to organize a mental health service in Scotland, but that it should be given credit for its pioneering efforts to interest and educate the public on the subject of mental illness and mental health, and that it is not too much to claim that its members were the originators of a mental hygiene movement in Scotland.

The Royal Commission on Lunacy in Scotland which was appointed on 3 April, 1855 published its report in 1857. Its terms of reference were to enquire into the condition of lunatic asylums in Scotland, and the existing state of the law in that country in reference to lunatics and lunatic asylums. The report, which bears testimony to the intelligence, industry and humanity of its authors, dealt with the following matters:

It dealt with the existing law of Scotland on the subject of lunacy; secondly, it contained a statement of the number of insane persons at that time in Scotland and the manner in which they were distributed; thirdly, it investigated the accommodation provided for the insane, whether in public asylums or in private establishments recognized by the law, and dealt with the condition of these establishments and the treatment of the patients confined in them; fourthly, the report contained an account of the conditions of insane persons not confined in these establishments as far as they could be ascertained; fifthly, it described the manner in which the law had been administered, with special reference to any abuses that had been found to exist, either owing to defective administration of the present law or because new legislation was required; and, lastly, the report contained recommendations as to the legislative measures required.

I have no time to deal with the law of Scotland on the subject of lunacy at the time of the Commission's investigation, except to say that it seems to me to have been adequate had it been properly administered.

As to the number of insane at that time and the manner in which they were housed, the Commission estimated that there were 3,328 insane persons under the protection of the law.

There were many insane persons, however, who did not come into this category, and the Commission had considerable difficulty in estimating their number.

It estimated that the total number of insane in Scotland at the time was 7,403 and of these 3,736 were males and 3,667 were females. Of that total they estimated that 2,603 were congenital idiots and 4,800 were lunatics.

With regard to the social position of the patients, 2,732 were private patients and 4,642 were paupers, and 29 were criminal lunatics. It was estimated that of the total number 768 could be regarded as curable and 4,032 as incurable.

The population of Scotland by the census of 1851 was 2,888,742, so that on the basis of the figures quoted there was at that time one insane person to every 390 of the population.

The accommodation provided at that time for cases of mental illness consisted of the chartered mental hospitals, of which there were 7, one each in Aberdeen, Dumfries, Edinburgh, Dundee, Glasgow, Montrose and Perth. In these public or chartered asylums there were 2,132 patients.

There was only one public asylum without a charter, namely, the asylum in Elgin which received only pauper patients and contained in May, 1855, forty patients.

In licensed poorhouses, of which there were twelve, there were 423 patients, and in licensed private houses, of which there was the astonishing number of 24, there were 657 patients.

There were 41 patients in what were called reported houses, 29 in prisons and 15 in schools for idiots.

In houses in which the insane were received without the knowledge of the Sheriff, which included unlicensed poorhouses, private houses and unlicensed private establishments, there were in the unlicensed poorhouses 253, in private houses not licensed by the Sheriff 3,798 and in other unlicensed private establishments 24, so that a total of 4,750 patients were being cared for without any legal provision of any kind.

The Commission found much to criticize in the administration of the law. They found that the visits of the Sheriff and of the Medical Inspectors proved quite ineffective in the prevention of gross neglect and improper treatment of patients. These visits were too infrequent, the inspection was insufficiently searching and in many instances the visit had become a mere formality.

The Medical Inspectors appeared to take little interest in their duties. They were frequently changed, so that they could not be expected to take any permanent interest in the patients in the licensed houses which they visited.

The books which the law enacted should be kept in the licensed houses were frequently not kept, or if they were kept the entries were improperly made.

Although restraint was extensively used in the licensed houses, the Commission failed to find a register of restraint in any licensed house in Midlothian.

They criticized the remarks which the Sheriff inscribed in the book on his visit. These, they thought, were often of a vague character and seldom contained recommendations or suggestions about improving the condition of the patients.

They thought that little reliance could be placed upon the Inspector's report and that they bore little relation to the actual establishment.

In one licensed house in Lilybank, Musselburgh, where manual restraint was much used, the column for entering cases of restraint was entirely omitted from the record, and yet the book was regularly signed by the Medical Inspectors without comment.

The books kept in the licensed houses were either not kept or if entries were made in them these entries were of no value as far as they gave any indication of the nature of the treatment given to the patient.

Although, according to the law, Justices of the Peace in every county might nominate three of their number to visit and inspect private mad-houses, in only one instance did the Commissioners find that nominations had been made, and in this case the Justices had failed to visit.

They found that the visit of relatives was of little value in preventing the ill-treatment of patients because these relatives were either apathetic or ignorant.

Inspectors of Poor rarely visited their patients and when they did the owners of the houses prevented them from seeing the true state of affairs. They saw the patients in public rooms and they were rarely allowed to visit the patients' quarters.

The Lunacy Laws were obscure in some respects and difficult to follow.

Dr. Skae of Morningside in his evidence confessed that he did not know the law on the question of who should authorize the discharge of pauper patients. He thought that the power lay with the Inspectors of Poor and he said he invariably refused to allow relatives to remove a patient without the authority of the Inspectors.

It was found that Inspectors frequently removed patients from one place to another for reasons of economy against the opinion of the Medical Officer of the hospital. As a result of this policy a large number of patients were removed from the chartered asylums to private licensed houses, to poorhouses or to their own homes.

For instance, it was found that pauper patients in the Murray Royal at Perth could be maintained more economically in a private licensed house in Musselburgh. They were immediately transferred, without the knowledge of the Sheriff and without the knowledge of their relatives, many of whom only heard of the transfer when they applied to the asylum in Perth to visit their friends. The Board of Supervision was ignorant that the transfer had been made.

It was found that the patients who were in good bodily health at the time of their removal quickly deteriorated and that the mortality rate among them was very high.

An Inspector of Poor was asked, when giving his evidence before the Commission, about the inspection he made of the premises to which the patients were to be transferred, and he admitted that he did not look at their bedding and that "this was a neglect", and he did not ask where the patients were to wash themselves or what they were to wash in. He did not see whether they had any day-rooms to sit in. He did not see whether they had anything to sit on and he admitted that this should have been looked into. He did not see any fires. He could not be certain that two or three were not kept in one bed.

Some of these patients died without the knowledge of their relatives whose addresses had not been given to the proprietor of the houses, nor was the Inspector of Poor informed of this when the patients became sick.

Of the attitude of the Parochial Boards, one of the witnesses, Sir Andrew Allison, in his evidence said, "Economy is the great thing Parochial Boards look to. I don't think they almost ever look to anything else." "Parochial Boards," he said, "would send patients to a cheap house even if one a little dearer were better in every respect. Economy is, in fact, their chief object."

Disastrous results sometimes followed from the removal of individual patients from properly conducted hospitals to private houses.

A pauper patient of the Parish of Lochgoilhead was removed, after a residence of four years, from Gartnavel. He was regarded as a dangerous person. He was placed by the Inspector of Poor in the poorhouse in Greenock, where before long he killed one of the other inmates. Another patient, described as an idiot, was in the Murray Royal Asylum in Perth. He was removed by the Inspector of Poor and placed in the Aberdeen Royal Asylum. From there he was again removed by the Inspector of Poor who placed him to board in a cottage. One day while out walking on the road the patient seized a child by the legs and dashed its brains out against a tree.

Sometimes patients endured great hardship in their transport from their homes to the asylums. They frequently arrived at the asylums bound with ropes and in a state of great discomfort and pain. Female patients were sent to asylums under the sole charge of an inspector or a constable. Dr. McIntosh, the Superintendent of Gartnavel, speaking of patients received from the Western Highlands said, "They generally arrive bound and I have seen the flesh cut." And Dr. Skae of Morningside said, "All the patients coming from the North are generally in a hopeless state, and all male patients coming from Leith have their hands tied behind their backs. Patients from the Northern counties are generally bound with canvas on their arrival and I have frequently seen ulcerations produced by ropes." One young woman admitted to the Perth Asylum had been tightly strapped to a window shutter for several days before her admission. Her wrists, fingers and ankles were oedematous and covered with ulceration and she lost the use of a finger by suppuration and disorganization of the joint. One more example will suffice. A female patient admitted to Montrose Asylum in 1855 arrived with a strong piece of wood inserted bit-wise between her teeth and firmly secured by a strong cord tied behind her neck. As a result of this her tongue ulcerated and although she improved in her mental condition she was left with an impediment of her speech as a result of the loss of a large part of her tongue.

It is no wonder that the Royal Commission commented that "the steps adopted in removing a patient to an asylum are, we feel, too often calculated to excite a degree of terror in the mind of the sufferer". The treatment of the case should be started the moment the patient was taken from home "for," said the Report, "his conception of the place to which he is to be conveyed must, in a very great degree, depend upon the steps adopted towards him in his removal".

In their comments upon the accommodation provided for patients the Commissioners found the worst conditions to exist in the private licensed houses, in which there was much evidence of neglect, squalor and ill-treatment.

Although some of the proprietors of these houses were medical men, many were laymen who had no knowledge whatever of mental illness or its treatment. The proprietor in one house in Musselburgh had previously been a grocer, another had been an unsuccessful baker, another had been a gardener, and one woman who became a licensed house proprietor had been a public-house keeper.

Only one house, namely Saughton Hall, had been built as an hospital. Most of the houses were overcrowded. They were grossly deficient in furniture and the sanitary arrangements were in many instances deplorable.

Many of the houses had no sitting room accommodation. The rooms were unprovided with seats and the beds were used as substitutes. Even tables for dining were, in some instances, not provided and the meals were served in a slovenly manner, the patients eating their food sitting on their beds, squatting on the floor or in corners of the airing court.

In Hillend Asylum near Greenock, a private licensed house, two patients paying £53 and £35 per annum respectively, a sum which the Commissioners thought should have secured them comfortable accommodation, were sharing a room with another patient, and for a month they had slept entirely naked in a miserable trough bed on a small quantity of loose straw. Both patients were dirty in their habits and the straw was found to be filthy and saturated with urine.

Nearly all the licensed houses were overcrowded. One witness, in his evidence, when asked about the absence of a fire in a house in Musselburgh said, "Indeed, fires hardly seem necessary from the overcrowded state of the patients." Another witness, speaking of the Musselburgh houses, said, "Unless there were a good many patients they would not pay at all; there is no doubt of that. If a sufficient amount of space were given I don't think it would pay." And he added, "The Parish try in general to get the payments as low as possible without caring one farthing how the patients are taken care of."

Sometimes these houses contained no fireplaces and even where fireplaces existed they were boarded up.

The patients were usually poorly clad. Patients were allowed to lie on urine-soaked straw mattresses for several days. Sometimes they slept on loose straw on the floor, covered with a sheet, on the straw alone, and sometimes the quantity of the straw was so little that their bedboards were scarcely covered. Many of the patients slept naked.

Restraint and seclusion were much used. Some of the patients were constantly manacled. The strait-waistcoat was in daily use and restraint was applied at the discretion of the attendants. Appliances for restraint in the form of handcuffs, leg-locks, straps and strait-waistcoats were found to be hanging in the ward so that they could be applied by the attendant when he thought it was necessary.

A strong feeling of family loyalty and affection, a fear of institutions and, above all, a horror of becoming pauperized, resulted in many insane persons being kept at home with their families or boarded out with relatives or friends. The condition of these patients was in many instances deplorable. In the Parish of Dysart in Fife two patients were found living with relatives in a two-roomed house. The bed frames consisted of loose and irregularly placed rough boards. There was no mattress, not even loose straw. The coverings were mere rags. The floor was damp earth and the outer room in many parts an inch deep in water. A chair, a ricketty table and a cupboard constituted the entire furniture. There was no means of cooking food and no place or crockery of any kind to hold it. The window of the front room had no glass and was closed by a wooden board. The whole house presented a most depressing picture of dirt, wretchedness and want.

In another reported on by the Procurator-Fiscal at Dingwall the patient, a male pauper lunatic, aged sixty-eight, lived in the hamlet of Auchentee, about forty-eight miles from Dingwall. He had been insane for forty years. He lived in a turf house, the roof was leaking and the door about four feet high opened directly into the place where the patient was confined and there was no window or any opening for one. The turf walls were damp and the floor was of earth. There was no furniture of any description except the bed to which the patient was chained. No bedding except a quantity of loose straw was provided. The patient was wrapped in a piece of blanket, old and dirty, and two pieces of old bed covering. Except for these bits of rags he was naked. He had been chained for thirty years. The chain was two and a half feet in length and its end was fastened to the end of the bed with an iron staple. The other end was fastened round the patient's ankle. He never left his bed. His knees were now contracted and drawn up to his chest and completely rigid. He was stated to be occasionally "furious and excited". He never washed except twice in the course of the year. His sister, who looked after him, was in receipt of 12s. 6d. per month from the Parochial Board.

In many counties in Scotland all types of cases of mental illness were received into poorhouses, and in many instances the arrangements for their treatment were quite inadequate. The premises were often small and poorly constructed. The rooms were insufficiently furnished. The wards were often overcrowded. Sometimes two patients occupied the same bed. The bedding of deteriorated patients was often soiled. Restraint was generally used and applied at the discretion of the attendant. Occupation and amusements were seldom provided. Statutory records were not kept in some of the poorhouses. The Commission's Report commented on the high mortality rate in poorhouses as compared with the mortality rate in the chartered hospitals. The Commission strongly disapproved of the tendency to attach wards for mental patients to poorhouses.

In its comments upon the chartered hospitals, which were generally favourable, the Report paid tribute to the benevolence of the private individuals who had provided the money for the erection of these institutions. "No country proportionate to its population has voluntarily done so much for the insane and, although it may be said that Scotland presents an unfavourable contrast with most civilized states in not having a national institution for the reception of its insane poor, yet as regards those erected by private benevolence it may claim a marked and honourable distinction."

Most of the chartered hospitals were well constructed and provided good accommodation for the patients, but the report contained criticism of the internal arrangements of certain institutions.

The erection of more simple buildings was advocated, having a more domestic atmosphere and arrangements. It was thought that space was wasted, and as an instance of the disadvantages of extensive galleries the evidence of Dr. Rainey was quoted. Speaking of the Paisley paupers at Gartnavel he said, "They wish to get back to Paisley; they feel themselves lost in Gartnavel."

These poor "Paisley buddies" were apparently overwhelmed and oppressed by the spacious galleries of Gartnavel; and the Commissioners commented, "In such plain domestic buildings a more contented frame of mind is likely to arise, which is highly important and conducive to mental restoration."

Even at that time some of the chartered mental hospitals were overcrowded, and the Report commented that this resulted from a wish on the part of the Boards of Management to meet the pressing needs of the community.

The Royal Commission was not altogether happy about the management of the chartered asylums, on the grounds that usually the Directors took little direct part in the management of the asylum and few of the contributors attended the annual meetings of the Directors, so that there was a tendency for the management to be carried out by a few individuals with little or no check on their management by the public. The Directors were thus, without any blame being imputable to them, in a great degree an irresponsible body, there being little or no check on their proceedings on the part of their constituents or the public.

Although the hospitals were generally well conducted, it was thought that occasionally mistakes were made and they were very doubtful about the wisdom of the Directors of Gartnavel who, in their zeal to extend the benefits of the institution had incurred a debt of nearly £40,000 in order to extend the hospital; thus preventing the introduction of improvements which the Medical Superintendent wished to make.

It was thought that the Directors of the hospital at Morningside were likely to fall into a similar error.

The Report commented that the Medical Superintendents in the chartered asylums had virtually plenary powers, though subject to the control of the visiting committee of the Directors, but they made no criticism of this state of affairs.

The Commission was of opinion that some of the chartered hospitals were not economically conducted, and because of this the charges for patients were too high.

As to the treatment of patients they found that in general they were well clothed, although in one of the chartered hospitals dirty and destructive patients were permitted to be entirely naked while in seclusion. The beds were clean and comfortable, but the Report condemned the use of straw as bedding. They were not impressed with the arrangements made at Gartnavel for the care of patients of deteriorated habits, whose beds stood over sinks or leaden troughs sunk in the floor.

The Commission thought that notwithstanding the very creditable manner in which the chartered hospitals were on the whole conducted, Superintendents had not yet entirely succeeded in their efforts to act upon the modern views of treatment of the insane; however, it was admitted that they had difficulties to contend with and that they deserved much credit for what they had accomplished.

Although the diet of the private patients was varied and abundant there was reason to criticize the diet of the pauper patients, although on the whole it was probably better both in quantity and in quality than that of the Scottish peasantry in general.

Personal restraint had almost entirely disappeared in the chartered asylums, but seclusions for long periods was frequently used. One of the witnesses, Sheriff Allison, said that he had seen more seclusion in Gartnavel than anywhere else.

Amusement and recreation was provided for the patients in the form of games, frequent excursions, occasional picnics, concerts, lectures, evening parties and dances; and at the Crichton in Dumfries there were also theatrical performances. The Commission however commented that some Medical Superintendents had been content to provide entertainments to the exclusion of more serious occupations.

The Report commented favourably on the museum of natural history in the Crichton Royal in Dumfries and on its library, which contained 5,000 volumes.

On the basis of their most searching investigations the Royal Commissioners came to the conclusion that the Lunacy Laws as they then operated in Scotland were unsatisfactory and that they did not give sufficient protection to the lunatic and they recommended that the existing statutes should be replaced and that a new code should be introduced.

Their Report recommended the erection of district or county asylums for pauper lunatics, which should include accommodation for the insane belonging to the labouring classes who were not strictly paupers. It also recommended that there should be more suitable accommodation for criminal lunatics.

In order that the law should be properly administered it recommended the creation of a competent Board, invested with certain duties and responsibilities to whom the general superintendence of the insane in Scotland should be entrusted, including powers to license houses for the reception of the insane, to visit all asylums, licensed houses, poorhouses and houses containing only single patients; to order the removal of patients to or from an asylum, or from one asylum to another; to give leave of absence to convalescent patients; to regulate the diet in asylums and licensed houses for pauper patients; to make regulations for their management with direction to report to the Secretary of State for the Home Department.

The Government of the day accepted the Commission's report and promptly acted upon it, with the result that an Act of Parliament entitled "An Act for the Regulation of the Care and Treatment of Lunatics, and the Provision, Maintenance and Regulation of Lunatic Asylums in Scotland" received the Royal Assent on 25 August, 1857; and under the terms of the Act a General Board of Lunacy, consisting of five Commissioners, was appointed.

Of these Commissioners two were medical men: James (afterwards Sir James) Coxe, and W. A. F. Browne.

I think there can be little doubt that the policy of the Board of Lunacy, at the time under consideration, was founded on the views of Drs. Coxe and Browne. Both were men of high intelligence and wide cultural interests, who would at any time have been accepted as outstanding men and as leaders in their profession.

Further, it happens that both were greatly influenced in their ideas by two remarkable men, the brothers George and Andrew Combe.

The Combe brothers, Andrew and George, were known in their time not only for their writings on phrenology but for their philosophical, educational and philanthropic interests.

George Combe was born in Edinburgh in 1799. He became a lawyer and a writer to the signet, but he is best known for his writings on phrenology, philosophy and education.

He was the author of *The Constitution of Man*, a philosophical work based on phrenology. His numerous writings on education were published in a large volume edited by William Jolly, one of His Majesty's inspectors of schools, and published in 1879. In his preface Jolly describes Combe as one of the most enlightened and enthusiastic educationists this country has produced.

Combe was a man of wide interests. He was keenly interested in all humanitarian reform and he wrote about the humane treatment of the insane and upon the reformation of criminals. His wife was Cecilia Siddons, a daughter of the great actress. His name is commemorated in the George Combe Psychological Laboratory in Edinburgh.

His younger brother, Andrew, was a student at the Surgeons' Hall, Edinburgh. After completing his medical studies there, he went to Paris where he became interested in phrenology and he made numerous contributions to the *Journal of Phrenology*.

He practised medicine in Edinburgh, and among his other works his *Observations on Mental Derangement*, published in 1831, attracted much attention. This book was republished in an abridged form in 1887 under the editorship of Dr. Arthur Mitchell, one of the Commissioners in Lunacy for Scotland. Dr. Mitchell gives us a clue to his own views on phrenology when he says in his preface that the fundamental principles of phrenology may be considered as no longer in dispute. He also claims that Dr. Combe's advocacy of benevolence in the treatment of the insane had a large influence in shaping the existing lunacy laws of England and Scotland. In the section of the book devoted to the treatment of mental disease, Combe says, "the more nearly we can approximate our treatment of the insane to that of reasonable human beings the greater will be our success".

He also wrote a most detailed manual on the physiological and moral management of infancy and Dr. Mitchell says that there was still a steady demand for this book at the time in which he was writing in 1887. Combe suffered from pulmonary tuberculosis for many years, and died in 1847.

Andrew's life was written and his correspondence published by his brother, George.

Young Andrew had some difficulty in deciding upon his career. When he was asked by his family what profession he would like to follow, his reply invariably was, "I'll no be naething."

It was decided, however, that he should be apprenticed to a Mr. Henry Johnston, a member of the Royal College of Surgeons, and on 9 April, 1812, on the day on which he was to start his apprenticeship, he refused to leave the house and after all persuasion had failed it was decided by his family that compulsion would have to be used and he was forcibly dressed and carried bodily by his father, his brother George and his younger brother pushing him from behind, for several yards along the high road before he finally decided to give up the struggle and allow himself to be led to the College of Surgeons.

He seems to have entered into his studies with enthusiasm and he not only gained a medical qualification but he obtained some eminence in his profession.

In 1834 he visited Hanwell Asylum and in a letter to Miss Coxe he spoke in the highest terms of what he had seen there. He commented particularly on the benefits resulting from the useful employment of the patients and of the consideration given to their likes and dislikes. He praised Dr. Ellis, the resident physician, and his wife, whose influence in calming and cheering the patients he thought was very great. He found that Dr. and Mrs. Ellis were phrenologists and he said he was pleased to find the principles enunciated in his book on insanity vindicated by the practice in this establishment.

The post of Physician to the Montrose Asylum aroused Combe's interest, but before making application for it he asked his brother George if he could discover for him what were the duties of the post and "if the person appointed was to control or be controlled". When, however, Dr. W. A. F. Browne told Combe of his intention of applying for the post, Combe not only gave up his intention of becoming a candidate but he gave all his support to Browne, who was appointed.

In a letter to Sir James Clark on the importance of hygiene, he expressed ideas which closely resembled those expressed by his nephew and his pupil, Sir James Coxe, in his Presidential Address to this Association. Here is one quotation from the letter, "What an influential part the state of mind and general mode of life perform in the production and cure of disease, and yet how little the medical men interest themselves in the feelings or social position of their patients so as to discover either what they feel or what they suffer. How little pains are bestowed in cultivating confidence and affording sympathy . . . What a powerful hygienic instrument is the physician himself and yet how few know it." He suggested that the physician should not only concern himself with the cure of the individual patient but that he should accept responsibility for the happiness and welfare of the patient's family.

Among his appointments were those of Physician Extraordinary to the Queen in Scotland. He was also a Manager of the Morningside Asylum and in his will he bequeathed £50 to the hospital. He resigned his office in 1840 because apparently he felt that he could not carry out the detailed inspection of the hospital which he thought his office required. He took his duties very seriously, for he thought that they included not only frequent visits during the month but the investigation of individual cases and "an enquiry into the means, moral or medical" which were being used to influence them. These investigations were to be made in the absence of doctors and nurses.

When he was still a manager of Morningside he wrote a letter expressing his opinions on the qualifications required in a Physician Superintendent of an institution. He thought that "a Physician Superintendent should possess the physical strength, the natural activity and the mental energy, without which constant intercourse with the insane becomes a drudgery instead of a labour of love and moral interest". He thought it was on the resident medical officer that the success of every asylum, as a means of cure, must ever mainly depend. "With common kindness and common sense it is not difficult to present the external features of order and comfort, but it is an order which is constantly in danger of falling into lifeless routine and which leaves many a patient to move on in the dull round of disease who, by individual care and attention, might have been roused to healthful hope and activity. To the patient himself the difference is very great between feeling himself individually the object of an intelligent and ever-active sympathy, and being only one out of many, all treated kindly but with no regard to peculiarities of character or condition."

He was opposed to the employment of lay Superintendents which, at that time, it was proposed to introduce in the public asylums in Ireland. He thought that such a step would put a stop to the improvement which had been going on so rapidly for the last twenty years.

Combe wrote this about himself: "I had an early and great veneration for moral excellence and after having been cold or sullen in the days of my earliest youth, I have gone to bed and cried for want of moral sympathy and formed strong resolutions to be for ever after kind and good no matter how others might treat me."

It is clear that Browne and Coxe entered into their work as Commissioners of the Board of Lunacy with a sense of mission. They were both reformers and they found an outlet for their zeal in improving the conditions of the insane in and out of hospitals. They were convinced that the diseases and vices of mankind could be greatly alleviated, if not cured, by civilization. They had a strong desire to do good and they had no doubt that in doing so they were improving and elevating society. They were optimists in that they believed in human progress. As reformers they were not bigoted, repressive or intolerant.

They believed that most of the evils in society were attributable to ignorance and stupidity and not to deliberate cruelty, and they thought that by education and example they could dispel ignorance and reform evil doers. They had much pity for the oppressed but they had also understanding of the oppressor whom they did not wish to destroy but to educate and reform.

Browne had gained practical experience of the subject as physician to the Montrose Asylum and as Superintendent of the Crichton at Dumfries.

Coxe's knowledge was more theoretical and perhaps for this reason his views were less orthodox. His Presidential Address at the meeting of the Medico-Psychological Association in Edinburgh in July, 1872 is said to have startled his audience by the boldness of the views which he enunciated.

James Coxe was the son of Robert Coxe of Gorgie, Edinburgh where he was born in 1811. George and Andrew Combe were his uncles, and because of the death of his father at an early age, Coxe was reared under their guardianships. He was a graduate in medicine of Edinburgh University and he also studied at Göttingen, Heidelberg and Paris. Although he practised medicine in Edinburgh for a time, much of his activities was directed towards the revision and editing of his uncles' works on phrenology.

His valuable work as a member of the Royal Commission was recognized, and it was natural that when the Board of Lunacy was instituted he should be made a member of it.

He is described as being of a genial disposition and having a "quiet humour which enabled him often to effect by a joke that which could not be accomplished by an argument; thus he could induce officials of the institutions which he supervised to undertake what seemed to them to be dangerous or impossible tasks, converting them to his views by his own experience".

His wife, who was a daughter of Dr. Cumming of Logie, is said to have been the original of Burns's "Bonnie Lesley".

His Presidential Address to this Association in 1872 may be described as a plea for mental hygiene. Indeed it is possible that he was the first to use this term, which he did in this context. "The medical profession," he said, "alone are trained in a knowledge of the structure and functions of the human frame, but even their education is frequently very imperfect especially as regards the preservation of health. It is in mental hygiene, however, that this deficiency is most apparent."

He disagreed with the view that insanity was a disease of civilization. "It was," he said, "the want of civilization which caused insanity." He drew a parallel between insanity and crime which he attributed to the neglect of moral and industrial training. He said that the line which separated insanity and crime is artificial and unreal; "asylums and jails were antidotes which the state provided to redress the effects of its neglect." He thought "it would be difficult to show good reasons for the practice of extending to the inmates of asylums the benefits and indulgences which are withheld from the inmates of prisons". He did not think that there was a sharp dividing line between sanity and insanity. What might be a delusion in one cultural setting might in another be a religious dogma.

He spoke of the powerful effects of early impressions upon the formation of personality and he emphasized the importance of the education and moral training of the young. He criticized the educational system in the schools. "It is seldom," he said, "that schoolmasters have any acquaintance with the physical, intellectual or moral organization of beings entrusted to their care.

Moral and physical training," he said, "scarcely receive any attention." He was critical of the clergy. He questioned whether a strict religious training based on a mere knowledge of the doctrines of the shorter catechism yielded satisfactory results. He thought that the clergy spoke in a language which was unintelligible to their listeners, and he suggested that they should copy the example of the evangelical preacher, Spurgeon, and appeal to the intellectual and moral faculties of the congregations in common language, and deal with such topics as the duties and rights of each man in his respective social position. Sermons, he thought, should include an exposition of the wonders of creation, the duties of parents to children, or children to parents, of masters to servants and of servants to masters. Any educational system should include an explanation of the moral obligations of treating the lower animals with kindness and consideration. He agreed that asylums were indispensable institutions, but he thought that many inmates of asylums might, nevertheless, be better in the outside world. He did not agree that asylums always humanized the patient where they failed to cure him. Even in the best conducted asylum the patient's life was restricted and there was much in ordinary life, in its change of society, amusements, scenes and circumstances which helped to lift the mind out of its diseased rut and to restore it to healthy action. He did not think that an asylum possessed any special virtue. He thought that "medical men devoted to the treatment of insanity injured themselves and the profession in the estimation of the public when they made exaggerated claims for the success of their treatments, or when they maintained that some special or extraordinary genius, or some special or extraordinary attainments were necessary for the treatment of mental illness".

He reiterated this view in his evidence before the Select Committee of the House of Commons on Lunacy Law in 1877*. When he was asked if he thought that it would be an additional protection to the patient if all dealings with lunatics, or alleged lunatics, were in the hands of specially educated medical men, he replied that he thought "the practice would be very apt to degenerate into a close guild of specialists who would be regarded by the public with distrust".

He did not agree that the early admission of cases of mental illness to asylums always yielded good results. He thought that equally good results might be obtained by treating the patient at home. The asylum was simply a convenient hospital for treating cases of mental illness, but after a time it became a convenient prison. He did not think that patients were improperly detained in asylums, but he thought that there were many cases which would be perfectly well treated outside. "I think," he said, "it is a very hard case for a man to be locked up in an asylum and kept there. You may call it anything you like but it is a prison and he is cut off from all associations of outdoor life. A man has his life only once and it is a very hard thing to keep him in an asylum all his days."

He thought that a great deal of the supervision of a good asylum was not medical. He thought it was like the management of a large hotel or something of that kind and medical men, he thought, were not necessarily the best hotel or farm managers. He saw no objection to certain mental hospitals having a lay Superintendent. He was in favour of small asylums. He would prefer that the number of patients should not exceed 200.

In his Presidential Address he criticized what he described as the fashion of the day to seek to regulate the conduct of people by legislative enactments. He thought that in many ways the liberty of the subject was curtailed by statute in the hope of counteracting evil habits and promoting virtuous conduct. He deplored this tendency and he instanced the prohibition under the licensing laws in Scotland on the service of drink in public houses on Sundays except to *bona fide* travellers. He felt that drunkenness was not to be combated by legislation but by education.

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* Minutes of Evidence, p. 99, Q. 2064 ff.

William Alexander Francis Browne was born in Stirling in June, 1805. His father, Lieut. William Browne of the Cameronian Regiment, having been lost at sea at the age of twenty-one, Browne was brought up by his paternal grandparents in Stirling. He attended the High School there and later he studied medicine at Glasgow University. He spent a period of study in France under Pinel and Esquirol, and, on his return to Stirling in 1830 he taught in the Edinburgh Extra-Mural Medical School, while at the same time he was in general practice in Stirling.

In 1834 he was appointed Medical Officer to the Royal Asylum, Montrose, and in 1838 he took up his duties as Superintendent of the Crichton Royal Institution in Dumfries, a post to which he had been nominated by the patron of the asylum, Mrs. Crichton, who had read Browne's book *What Asylums Were, Are and Ought to Be.*

In 1857 he was appointed one of the two Medical Commissioners in the Scottish Board of Lunacy.

He married a daughter of Dr. Andrew Balfour of Edinburgh.

In 1870 he was thrown from his carriage and his injuries are said to have caused him to develop glaucoma. Complete loss of eyesight necessitated his resignation from his post on the Board of Lunacy. He retired to Dumfries, and he died in 1885.

In early life Browne became interested in phrenology and he is said to have assisted George Combe in his phrenological studies. He developed a close friendship with Dr. Andrew Combe and his book published in 1837 entitled *What Asylums Were, Are and Ought to Be* is dedicated with sincere respect and gratitude to Dr. Andrew Combe. In the copy of the book which I have borrowed there is an inscription dated 29 February, 1860 in the author's handwriting which reads as follows: "With great respect and kind regards from the author who thinks now as he thought twenty years ago."

The book consists of five lectures delivered to the managers of the Montrose Asylum, and in his preface Browne says that the object of his lectures is to "draw the attention of the public to what has been done and remains to be done for the relief of the most unfortunate of our fellowmen; for those who may be almost literally said to sit in darkness and in the shadow of death, being fast-bound in misery and irons."

The book is, in fact, a condensed treatise on mental illness, dealing as it does with the definition of insanity, its incidence with statistical data, the history of the treatment of mental illness and the history of mental hospitals. One chapter is devoted to a description of mental hospitals of the day and in his final chapter he describes his conception of what mental hospitals ought to be. The author concludes with a description of the ideal mental hospital—"A spacious building resembling the palace of a peer surrounded by extensive grounds and gardens, the interior fitted with workshops and music rooms, the sun and air allowed to enter unobstructed by shutters or bars. The inmates are actuated by the common impulse of enjoyment; all are busy and delighted by being so. The house and all around it appears a hive of industry." He gives a graphic and highly idealistic picture of patients engaged in work and play. "Some act as artisans, some rise to the rank of overseer, some work in the laundry and in the kitchens, some act as nurses, some are engaged in landscape painting and some in book-binding. They work in order to please themselves and having found joy in work, difficulty is found in restraining their eagerness and in moderating their exertions." That Browne thinks that such a hospital is not an impossible ideal is clear from the last sentence in his book which reads, "Such is a faithful picture of what may be seen in many institutions and what might be seen in all were asylums conducted as they ought to be."

In July, 1864 Professor Laycock's class in Medical Psychology visited the Crichton Institution, and Browne lectured to them,* choosing as his subject, The Moral Treatment of the Insane, which he defined as "every mode by which the mind is influenced through the mind itself in contradistinction to medical treatment in which the mind is acted upon remotely by material agents and through the body". He complained that there were officers still in charge of the insane who had not as much as heard whether there is a human mind or no. The regime in mental hospitals should aim at building up the ruined mind by training, education, discipline and by an appeal to the religious and intellectual faculties. He thought that an asylum should resemble as much as possible a private dwelling but that it should also be a grand moral school and reformatory as well as a hospital.

As an example of the type of hospital of which he approved he spoke of the magnificent District Asylum of Inverness which had no wall or fence around its extensive grounds.

He advocated useful employment for patients, "rather than frivolous diversions" and he suggested that patients should be paid wages which should be allowed to accumulate and be available to them on their discharge. He advised the abolition of what he called the "pandemonia called refractory wards" which he thought was a "mere concentration of all the elements of strife and disorder".

He favoured the nursing of male patients by female nurses in certain instances and he condemned the rigid segregation of male from female patients. "Promiscuous dancing," he said, "has repeatedly promoted physical as well as physiological changes, and general but wisely regulated intercourse tends to humanize and mollify the asperity of both sexes."

He spoke favourably of the experiment carried out in the York Retreat, where a body of women volunteers visited the hospital and associated with the patients. He emphasized the importance of the influence of the nurse upon the patient and he quoted Esquirol as saying, "First cure your attendant and when you have succeeded you may proceed to treat the patient."

He advocated music as a therapeutic agent. He quoted the case of a lady who "after hearing Scotch music retired to bed degraded, mute and fatuous. She rose next morning and remained permanently of right and rational mind, quietly remarking to the physician that the banks and braes o' bonny Doune had awakened her."

He suggested drama as a suitable outlet in cases of mental illness and he mentioned his own pioneer effort at the Crichton Royal in Dumfries in 1842.

He dwelt at some length on the qualities required in the Superintendent of a mental hospital, the government of which he thought should be

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* *J. Ment. Sci.*, October, 1864, **10**, p. 309.

"monarchical". The details as well as the principles should emanate from one central will, although the dictatorial powers of the Superintendent should be kept in check by a code of laws provided by the Governors, by Inspectors appointed by the country and by public and professional opinion and, above all, by the condition, tastes and character of those committed to his charge. "The person in charge of the hospital should feel that he is called to a mission, not to a practice, he must live with and for the insane, he must enter into their pursuits, pleasures and even their thoughts, and he must cherish a direct relation and intercommunication with the minds of those who, according to their nature, love him, fear him, depend upon him. He must compensate for the poverty and uncertainness of his remedies by the liberality of his sympathy, love and self-sacrifice."

The personality, the attitudes and opinions of these two medical commissioners are clearly reflected in the conduct and recommendations of the Board of Lunacy as set down in their early reports.

On the principle which ought to regulate the treatment of the mentally sick, they suggested that it should be "the provision of every comfort" which could reasonably be demanded to lighten the burden of perhaps the greatest calamity which can afflict humanity. They thought that legislation should be directed to facilitate as much as possible the reception of patients into asylums. They questioned the necessity of the Sheriff's order, which they said, although an absolute safeguard against the improper admission and detention of a patient in an asylum, contained no provision for ensuring discharge on recovery, and they thought that on the whole the risk of improper detention following recovery was greater than any risk of being improperly placed in an asylum. They were not, however, prepared to suggest that the sheriff's warrant should be abolished. They held that it was impossible to draw a distinctive line between so-called criminal insanity and other forms of mental aberration, and they therefore disapproved of the suggestion of the General Board of Directors of Prisons that a new asylum for criminal lunatics should be built in connection with the central prison in Perth. They considered it of great importance that every association which tends to connect insanity with crime should be obliterated, and for this reason they greatly regretted to witness a new criminal asylum in connection with a prison. "It would perpetuate the union which they greatly desired to see for ever broken." They saw no reason why many so-called criminal lunatics should not be treated in ordinary asylums and if there were cases which should not be allowed to mix with the ordinary patients special wards should be provided for them.

They advised the abolition of lunatic wards in poorhouses, "the primary object of which was to afford a test of poverty and to provide for the poor in the most economical manner".

We have seen that Coxe had some critical things to say about mental hospitals and their effects upon chronic patients.

This attitude is reflected in the opinions expressed by the Board. They thought that patients were sometimes admitted to asylums not so much for their own benefit as for the comfort of the patient's family, and they recommended that Superintendents should always be alive to the possibility of discharging patients when they were no longer a danger to themselves or to other people. The mere fact that they were technically insane should not be a good reason for their continued detention in the asylum. They advocated the discharge of patients on trial.

They were aware of the difficulties which arose in the case of alcoholic patients admitted to asylums in a state of acute mental disorder, who quickly improved so that they could no longer be legally detained and who left the hospital before they were cured of their addiction. They had, however, no solution to offer for this problem.

They drew attention to the disadvantages arising from the presence of dangerous lunatics, or what we would now call Fiscal cases, in mental hospitals and they pointed out that the restrictions placed upon the Superintendent of the asylum in dealing with these patients might place obstacles in the way of the discharge of patients who, although technically insane, might be harmless.

At the present day the upgrading of hospitals and institutions has received much attention. The Commissioners of the Scottish Board of Lunacy must have been the greatest upgraders in history. They were never satisfied with the existing conditions in hospitals; they were always suggesting improvements in accommodation, in diet, in the nursing of the patients, in their clothing, in the service of their meals, in their amusements and recreations and in their training and management.

The Commissioners' reports upon the hospitals visited testify to the searching character of their inspection. Nothing seemed to escape their notice and they always found something to commend or to criticize. Here are a few of their comments upon the hospitals visited: "The kitchens and laundries are clean and cheerful but the former are defective in neatness and arrangement. The latter appear neglected. Numerous complaints are still made as to the manner in which the food is served. Additions to the furniture have been made but there are places which are still bald and bare, scarcely coming up to the standard recognized when the establishment was erected."

They complained that in one hospital the male patients "had not been made familiar with a tablecloth". They said that attention to cleanliness was required and they recommended the introduction of salt cellars on the table. They thought the diet in one hospital could easily be made more varied and more palatable without any great increase of expense. They suggested the provision of pieces of carpets as bedside rugs.

In one of their reports upon Gartnavel they commented that the sleeping accommodation for patients was satisfactory and that this state of affairs had been accomplished in spite of the opposition encountered in the tendencies of twenty-seven dirty patients, nineteen epileptics, eight paralytics and seven burrowers. They complained, however, that many of the patients were left in idleness, that the hospital was overcrowded and that the temperature in the upper rooms and garrets of what was formerly the house for the medical assistants and which was then used as dormitories for pauper patients, was extremely low.

The nineteenth century was an age of reform. It was characterized by an attitude of humanitarianism and philanthropy. But the principle was universally accepted, although not perhaps often enunciated, that the poor had considerable responsibility for their poverty, and while it was recognized to be praiseworthy and creditable for individuals to exercise benevolence and charity, the existence of poverty and destitution was to be accepted as part of the natural order of society. A good man gave out of his private purse to the relief of the poor, but it was quite another matter to tax the public purse in order to relieve destitution, and even when it was recognized that there was an obligation to provide for the poor out of public funds, the obligation was a minimal one. The pauper could hardly claim to be better fed or better housed in an institution than he was in his own home.

This, however, was not the attitude of the Board of Lunacy. Again and again they pleaded for higher allowances and better conditions for patients boarded out under private care. They frequently criticized the austere conditions in which paupers were housed in the chartered hospitals, while in another part of the hospital private patients lived in well-furnished apartments.

The Commissioners were not fanatical levellers. They did not question the right of patients of the higher classes to enjoy comfortable conditions and the service of refined and polite attendants, but they held strongly that because the pauper lived in squalor in his own home that was no reason why he should not be well fed, warmly housed and provided with the amenities of civilization when he was in hospital or when he was boarded out.

The Board of Lunacy sometimes found itself called upon to act as assessor or arbiter in the case of disputants who could not reach agreement, as for instance when the Inspector of Poor in the parish of Lesmahagow complained to the Board that the Directors of Gartnavel had charged him £6 17s. 6d. for four suits of canvas, four pairs of canvas gloves and three pairs of canvas boots used by a patient between 27 August, 1860 and 14 January, 1861. Similar complaints were made by other Lanarkshire parishes of the oppressive attitude of the Gartnavel Board in its dealings with the parochial boards. The Board exchanged letters with the secretary of the Board of Management of Gartnavel, who put forward the plea that Gartnavel had no revenue from public funds and that it had to rely entirely on money received in respect of the board of patients and that unless it was given a free hand in respect of the charges it made for the maintenance of patients it would be impossible for the Directors to meet the expenditure of the hospital, including the interest on the £25,000 with which the institution was still burdened.

The Board of Lunacy was not impressed with this reply, for it pointed out that the present arrangement in Gartnavel appeared to them "simply to be a one-sided contract which the asylum considered itself at liberty to break whenever it was in its interests to do so". The Lunacy Board would appear to have had the best of the argument, for the Gartnavel Board made no reply to this letter.

What was the attitude of those affected by the Board's policies and criticism?

There is ample evidence in the early reports of the Board of Lunacy that the Boards of Management of hospitals treated the Commissioners' criticisms and suggestions with the greatest respect.

In a report by the Visiting Committee to the Managers of the Royal Edinburgh Asylum regarding the observations by the Commissioners in Lunacy on the Asylum, the Committee deal with the numerous criticisms made by the Commissioner. These criticisms include the lack of single rooms in the hospital, the cheerless character of the furnishings of the male wards, the lack of chairs and of clothing cabinets. Criticisms of the fire precautions, suggestions that sheds should be erected in the airing courts, comments on the frequency with which the attendants left the service of the hospital and criticisms of the wages paid to them. A suggestion that classes in reading and writing should be resumed, a recommendation that patients should be allowed all facilities for writing to the Board of Management and that their letters should not be censored by the Medical Superintendent, and improvements in the quality of the food, in its cooking and in its serving.

The Board of Management agreed with almost all the recommendations made by the Commissioners, and they end their report as follows: Although on one or two points they think the Commissioners have arrived at erroneous conclusions, they cannot conclude without expressing the obligation under which the Commissioners have laid the Managers for bringing under their notice so many suggestions calculated to promote the comfort of the patients and the welfare of the asylum, objects which the visiting committee will steadily keep in view.

In his evidence to the Select Committee of the House of Commons on Lunacy Law in 1877,* the Superintendent of a Scottish mental hospital, when asked his opinion on the Board of Lunacy said, "I think I am speaking the truth when I say it is not generally satisfactory to the profession", and he went on to say that the impression of the Medical Superintendents was that the Board interfered a little more than they might do in special matters of detail which might be left to the Medical Superintendents who were supposed to have the skill and experience necessary to deal with them.

The *Journal's* commentator expressed astonishment at this opinion for he said, "This must strike a stranger oddly, for if there is one thing more than another that seems characteristic of the Scotch Medical Commissioners and Superintendents, it is the friendly terms on which they seem to be when they meet at professional platforms", and he went on to suggest that the particular Superintendent who had criticized the Commissioners was influenced in his opinion by the attitude which the Board had adopted in the case of a certain patient who had been detained in his hospital for a longer period than the certificates of emergency allowed him to be. In an action against the Superintendent the patient was awarded £150 damages, the Board of Lunacy having informed his agents, as no doubt it was their duty to do, about the illegality of his detention. The sympathies of the commentator were with the Superintendent—the general impression was that the Scottish Board of Lunacy "did a shabby thing in telling tales out of school".

The attitude of the Board of Lunacy on the subject of the Lunacy Laws was liberal and enlightened. They thought that the Scottish Lunacy Laws bore too close a resemblance to the criminal law, and they suggested that it was necessary, if patients were to be protected and if their admission to mental hospitals was to be facilitated, that the law should be interpreted with some latitude.

They suggested that the Sheriff should not act in a judicial capacity, and that he should not refuse to grant an order for the admission of a patient to a hospital because he was dissatisfied with the medical certificates. On the contrary they suggested that the Sheriff should sign the order, and that it would be the duty of the Commissioners of the Board of Lunacy to scrutinize the certificates and to call for their amendment when they were defective, or to order the discharge of the patient if insufficient evidence of his insanity was produced. They thought that the necessity for obtaining the Sheriff's order deterred relatives from seeking early hospital treatment for patients.

They advocated the voluntary admission of patients to mental hospitals.

I suppose we tend to think of the Board of Control as being primarily concerned with the somewhat sterile but necessary task of administering the Lunacy Laws, but although the Board of Lunacy—in its early days—recognized the administration of the law as an essential task, there is little evidence that it regarded this as its primary function. Its real concern was to raise the standard of treatment of the insane inside and outside of institutions. In all matters relating to the welfare of the patient, the Board assumed full responsibility and its slogan might well have been, "the buck stops here".

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* Dr. James Gilchrist, of Crichton Royal, *Minutes of Evidence*, p. 194, Q. 4196 ff. See *J. Ment. Sci.*, January, 1878, **24**, p. 279 ff.

An important aspect of its work was the encouragement of local authorities to build new hospitals where these were required, or to make arrangements with the existing chartered hospitals for the admission of pauper patients. The Board approved and advised upon plans for new hospitals. The Medical Commissioners inspected the existing accommodation in public and in private hospitals and in poorhouses, and passed judgment on what they saw. The Board withdrew the licence to receive patients from private houses if the conditions continued to be unsatisfactory.

By demanding what might have appeared at the time to have been impossibly high standards in the housing, feeding, care and treatment of the insane in hospitals and in private dwellings, the Board of Lunacy must have done much, not only to improve the conditions in hospitals but to revolutionize the public attitude towards the treatment of those suffering from mental illness.

In their visits to boarded out cases in remote country districts, they must have done much to awaken the sleeping conscience of the public and to arouse men to a feeling of their responsibility to the mentally sick.

The magnitude of the work of the Commissioners and Deputy Commissioners in visiting and reporting upon cases throughout the whole of Scotland is revealed by the fact that in the two years 1858 and 1859, 3,527 patients in over 600 parishes and in 30 counties were visited and in addition to this the Board received reports upon 570 additional patients. I think there is no doubt that it was this part of the Board's work, which brought it into intimate contact with the patients and their relatives, that gave the Commissioners most satisfaction; and when they record, as they were frequently able to do, an improvement in the conditions of patients in private dwellings as a result of their advice and intervention, their satisfaction is evident.

In one of the early reports of the Board, Dr. Arthur Mitchell, one of the Deputy Commissioners, defines his own attitude to his duties with respect to patients living at home or under private care. He says that owing to the want of suitable institutions for the training and instruction of mental defectives he felt it was right to impress upon the guardians the duty of educating the patient and he says that he gave them instructions as to how this should be done.

In the third report of the Commissioners there are many instances of the improvements brought about as the result of the Commissioners' intervention in patients living in unsatisfactory conditions, either with relatives or their friends. One example will suffice:

The visiting Commissioner found a male patient of sixty-nine who had been insane for many years chained to a bed which he had occupied for thirty years. The house was a turf hovel; cold, damp and dark. As a result of his confinement and restraint the patient had developed contractures of his limbs. The man was removed to other accommodation on the recommendation of the Commissioner and when he was next visited in his new home he was found to be kindly cared for by his new guardians, his physical state had greatly improved and he was now able to feed himself and he did not require restraint of any kind. The comment upon this case is that "a very great improvement has been effected in this man's condition and the occurrence of a similar act of cruelty in this parish is hereafter all but impossible".

The reports on the condition of single patients made by the visiting Commissioner, Dr. Browne, during the year 1860 form an interesting social document showing as it does very clearly the deplorable conditions under which the poorer classes lived at that time.

Nowhere were the conditions worse than in the Western Highlands and Islands, and in his report on patients visited in the County of Argyll Dr. Browne found evidence not only of poverty and bad housing conditions but also of harsh and cruel treatment of patients by relatives or guardians. He discovered that in 24 cases the patient had been terrified into obedience by violence.

By instructing the relatives or guardians in the proper management of the patient, by persuading the Inspectors of Poor to give additional allowances where these were necessary, by changing the guardian in some instances and sometimes by the removal of the patient to an asylum and by persuading the local authorities to repair the dilapidated houses in which the patients lived, steady improvement in the living conditions and in the treatment of boarded out cases was brought about, so that in an Appendix to its Seventh Report the Board was able to say that the improvement in the condition of patients living at home or under guardianship "is not so rapid as might have been desired but it is steady and well marked and a large number of pauper patients living in private houses are in surroundings which are on the whole satisfactory".

A striking testimonial to the success of the visiting Commissioners' efforts is contained in an entry by the parochial surgeon in one of his visits to a degraded and demented patient. He says, "The mental improvement in this patient is remarkable. Idiocy converted into comparative sanity, and the improvement is solely attributable to his having been admitted as a member of the household and to the general elevation and treatment enforced by Dr. Mitchell."

In their work the Medical Commissioners of the Board of Lunacy appear successfully to have combined the functions of administrators, clinicians, teachers and social workers. I venture to suggest that their record is a remarkable one and that they deserve honour and remembrance.

I will conclude this fragment of Scottish medical history by a quotation from the writings of that great Englishman, Dr. Samuel Johnson, "To judge rightly on the present, we must oppose it to the past; for all judgment is comparative, and of the future nothing can be known . . . The present state of things is the consequence of the former, and it is natural to inquire what were the sources of the good we enjoy, or the evil that we suffer. If we act only for ourselves, to neglect the study of history is not prudent; if we are entrusted with the care of others, it is not just."

DEFECTS OF LEARNING ABILITY WITH MASSIVE LESIONS OF THE TEMPORAL LOBE

By

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In previous studies of patients on whom an anterior temporal lobectomy has been performed for the relief of temporal lobe epilepsy, it has been shown that, following removal of the dominant temporal lobe, certain specific defects of cognitive functions arise which are not present after removal of the non-dominant temporal lobe (Meyer and Yates, 1955; Meyer, 1957; Meyer and Jones, 1957; Meyer, 1959). The present study has been undertaken to find out whether destruction or damage to the same region by massive lesions such as tumours and large scars would produce comparable findings.

The above cited studies have demonstrated that, following temporal lobectomy, the dominant cases, as a group, display a severe impairment of auditory verbal learning, whereas visual and tactile learning remain unchanged. The removal of the non-dominant temporal lobe does not give rise to learning deficit in any modality. The dominant group is less efficient on some tests of intelligence, owing to specific disabilities; but their general intelligence is relatively unimpaired if assessed on tests not affected by these specific disabilities. Non-dominant operation has no immediate or long-term effect on general intellectual functioning.

Since the present report is mainly concerned with the auditory verbal learning impairment, it is pertinent to say a few words about its nature. The impairment is evident on the recognition as well as on the recall type of test. This finding, together with the fact that the defect in learning remains one year after the operation—when all nominal dysphasic symptoms have disappeared—means that the learning difficulty is not due to dysphasia alone. Thus the defect has been shown to be of acquisition and not merely of execution. The degree of impairment bears no close relationship to the extent of the operation nor to the age of the patient. It is independent of the general intelligence level or the pre-operative auditory learning ability.

For the purpose of the present study, eight cases of massive temporal lobe lesions were assessed on the same battery of tests as used for the temporal lobectomy cases. These cases provide an interesting supplement to our studies of patients submitted to anterior temporal lobectomy.

CASE MATERIAL

The salient features of our eight patients are listed in Table I. Five had lesions of the dominant temporal lobe and three of the non-dominant. The

TABLE I

Case Material

A. Cases with Lesions of the Dominant Temporal Lobe

Case No.	Age and Sex	Hahdedness	Nature of Lesion and Site	Pre-operative Symptoms	Operative Procedures	Result
I	36 Male	Right	Infiltrating malignant astrocytoma of anterior left temporal lobe judged 5 cm. diameter.	Frequent psychomotor seizures for 4½ years with olfactory and deja vu auras. Recent slight nominal dysphasia. No raised intracranial pressure.	Craniotomy with biopsy. Subsequently deep X-ray therapy.	3 years later still surviving with continued epileptic attacks.
II	46 Male	Right	Epidermoid of skull invaginating hinder part of left middle temporal gyrus over an area roughly 4½ cm. diameter.	For 13 years frequent attacks of bilateral headache preceded by visual scotoma and numbness of face. For 18 months 15 psychomotor attacks, with aura of aphasia and tinnitus. No raised intracranial pressure.	Craniotomy with complete removal of tumour.	Symptom free 3 years later.
III	27 Male	Right	Meningo-cerebral cicatrix 3 cm. diameter situated over lateral aspect of left temporal lobe just posterior to the pole with destruction of the affected cortex.	Compound depressed fracture at 11 years of age. At 18 years onset of both psychomotor and grand mal seizures with aura of genital and epigastric sensations, and also of tinnitus.	5 cm. anterior temporal lobectomy.	Symptom-free 1 year later.
IV	37 Female	Right	Large infiltrating malignant astrocytoma of anterior part of left temporal lobe.	Headaches from raised intracranial pressure for 11 months. Recent slight nominal dysphasia.	Craniotomy with biopsy. Subsequently deep X-ray therapy.	All symptoms and signs relieved. 6 months later.
V	16 Male	Right	Cholesteatoma 4-5 cm. diameter within temporal horn of left lateral ventricle.	Frequent psychomotor seizures with sickly taste in throat since age of 1½ years. No dysphasia or raised intracranial pressure.	Craniotomy with removal of tumour through small incision. No cerebral tissues sacrificed.	Relieved of epilepsy. No residue apart from minimal homonymous hemianopia.

B. Cases with Lesions of the Non-dominant Temporal Lobe

Case No.	Age and Sex	Hahdedness	Nature of Lesion and Site	Pre-operative Symptoms	Operative Procedures	Result
VI	24 Male	Right	Astrocytoma 4 cm. diameter occupying white matter of anterior part of right temporal lobe.	1 year focal somatic sensory attacks involving left side of body. For 4 months also psychomotor attacks with abdominal aura, smell, and sense of familiarity. Recently raised intracranial pressure.	8 cm. anterior temporal lobectomy.	2 years later a developed recurrence of raised intracranial pressure. Re-explored at another hospital. Cyst found but no tumour identified. 1 further year later reported as deteriorating with hemiplegia.
VII	48 Female	Right	Meningioma 2·3 cm. diameter by 1·5 cm. high arising from floor of right middle cranial fossa and invaginating anterior part of fusiform gyrus.	For 10 years frequent psychomotor attacks with psychic aura (visual).	8 cm. anterior temporal lobectomy followed by removal of tumour.	Convalescence marred in first 2 years by recurrent bouts of depression followed in third year by good recovery. No definite fits.
VIII	39 Male	Right	Meningioma 5½ cm. diameter arising from inner half of sphenoidal ridge and invaginating the right temporal pole.	Failing vision with left homonymous hemianopia.	Removal of tumour.	Died 2 weeks after operation due to internal carotoid artery thrombosis.

lesions themselves were varied including an extensive scar and seven neoplasms. Four of the neoplasms were benign, invaginating the temporal lobe rather than invading it. Three of these benign neoplasms were successfully removed, although one of them was first submitted to an anterior temporal lobectomy because of the mistaken impression that we were dealing with an intrinsic infiltrating tumour. Three of the tumours were malignant gliomas infiltrating the lobe, and one of these with a lesion of the dominant hemisphere (Case IV) responded well to decompression and deep X-ray therapy with disappearance of all symptoms and signs.

TESTS AND TESTING PROCEDURES

The pre-operative testing took place from 1 to 21 days before the operation and the post-operative assessment was carried out from 26 to 32 days after the operation. The intelligence tests used were: Wechsler-Bellevue Form I and Form II (Wechsler, 1944 and Wechsler, 1946 respectively). Mill Hill Form I and Form II (Raven, 1948), and Matrices (Raven, 1949). Form I of each test was administered pre-operatively and Form II post-operatively.

The following learning tests were used:

1. New Word Learning Test, N.W.L.T. (Nelson, 1953) which involves learning the definitions of unfamiliar words.
2. Auditory-Verbal-Recall, A.V.R.—test of learning pairs of words using the auditory modality and recall mode of reproduction.
3. Auditory-Verbal-Recognition, A.V.Rg.—as (2) but involving recognition.
4. Visual-Verbal-Recognition, V.V.Rg.—as (3) but involving visual modality.
5. Visual-Design-Recognition, V.D.Rg.—test of learning pairs of designs presented visually.
6. Visual-Designs-Recall, V.D.R.—test of learning designs presented visually and paired with pictures of common objects; the patient is required to reproduce the designs from recall.
7. Tactile-Designs-Recognition, T.D.Rg.—test of learning pairs of wire patterns using the tactile modality. The subject is blindfolded and the patterns are presented into his palms.

Each test has an equivalent form which was used post-operatively. Previous data indicate that the two forms are equivalent (Meyer, 1959). The scores on these tests represent the number of stimulus presentations before reaching the required criterion (three consecutive correct responses per pair). The tests have been described in detail elsewhere (Meyer, 1957).

Not all the patients were given all the tests and Case VIII was not reassessed after the operation since he died.

RESULTS

The overall results are presented on Table II, and are arranged so that cases with dominant temporal lobe lesions are grouped together for comparison with the non-dominant lesions. Pre-operative and post-operative findings are also compared. As far as intelligence test scores are concerned it will be seen that for each dominant case the "verbal" scores are lower than "performance"

TABLE II

Results of Pre-operative and Post-operative Assessment on Intelligence and Learning Data

A. Dominant Temporal Lobe Cases

Case No.	Intelligence Tests										Learning Tests													
	Wechsler Verbal I.Q.		Wechsler Permane I.Q.		Wechsler Full Scale I.Q.		Mill Hill I.Q.		Matrices I.Q.		N.W.L.T.		A.V.R.		A.V.Rg.		V.V.Rg.		V.D.Rg.		V.D.R.		T.D.Rg.	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
I	78	91	102	93	89	93	81	81	89	93	30	25	61	49	32	31	15	15	7	5	16	18	34	12
II	—	—	—	—	—	—	84	83	110	120	17	11	45	10	18	11	16	14	12	11	—	—	16	18
III	—	—	—	—	—	—	—	—	95	110	—	—	76	77	33	35	12	15	10	9	18	16	24	30
IV	103	111	120	120	112	117	—	—	—	—	20	11	71	17	28	10	16	9	8	10	32	15	39	34
V	84	79	90	96	86	86	—	—	—	—	—	—	22	20	15	14	9	11	7	5	12	11	12	11

B. Non-dominant Temporal Lobe Cases

Case No.	Wechsler Verbal I.Q. Pre	Wechsler Verbal I.Q. Post	Wechsler Permane I.Q. Pre	Wechsler Permane I.Q. Post	Wechsler Full Scale I.Q. Pre	Wechsler Full Scale I.Q. Post	Mill Hill I.Q. Pre	Mill Hill I.Q. Post	Matrices I.Q. Pre	Matrices I.Q. Post	N.W.L.T. Pre	N.W.L.T. Post	A.V.R. Pre	A.V.R. Post	A.V.Rg. Pre	A.V.Rg. Post	V.V.Rg. Pre	V.V.Rg. Post	V.D.Rg. Pre	V.D.Rg. Post	V.D.R. Pre	V.D.R. Post	T.D.Rg. Pre	T.D.Rg. Post
VI	115	114	98	89	108	101	89	91	109	107	8	7	19	17	10	11	16	17	6	16	—	—	28	19
VII	107	104	107	88	107	95	105	103	—	—	7	9	16	20	14	12	8	11	18	21	22	20	18	19
VIII	126	—	102	—	115	—	—	—	—	—	6	—	10	—	11	—	10	—	6	—	22	—	17	—

TABLE III

Z Scores on Learning Tests as Compared with Norms Provided by Temporal Lobectomy Cases Tested Before and After Operation

A. Dominant Temporal Lobe Cases

Case No.	N.W.L.T.		A.V.R.		A.V.Rg.		V.V.Rg.		V.D.Rg.		V.D.R.		T.D.Rg.	
	Pre*	Post†	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
I	7·03	+0·72	3·27	+0·63	−2·01	+0·36	+0·48	+0·75	+0·71	+1·10	+0·39	+0·34	−0·49	+0·80
II	2·58	+1·32	1·94	+2·45	−0·12	+1·25	+0·35	+0·85	−0·008	+0·25	—	—	+0·72	+0·39
III	—	—	4·51	−0·67	2·15	+0·18	+0·86	+0·75	+0·24	+0·53	+0·30	+0·34	+0·18	−0·41
IV	3·61	+1·32	−4·09	+2·12	1·47	+1·29	+0·36	+1·36	+0·55	+0·39	0·28	+0·38	−0·83	−0·68
V		—	−0·03	+1·98	+0·28	+1·11	+1·23	+1·15	+0·71	+1·10	+0·55	+0·54	+1·12	+0·86

B. Non-dominant Temporal Lobe Cases

Case No.	N.W.L.T. Pre*	N.W.L.T. Post†	A.V.R. Pre	A.V.R. Post	A.V.Rg. Pre	A.V.Rg. Post	V.V.Rg. Pre	V.V.Rg. Post	V.D.Rg. Pre	V.D.Rg. Post	V.D.R. Pre	V.D.R. Post	T.D.Rg. Pre	T.D.Rg. Post
VI	+0·05	+0·08	−0·02	−0·05	+0·53	+0·18	−0·65	−1·16	+0·38	−0·40	—	—	−0·25	+0·14
VII	+0·20	−0·73	+0·20	−0·35	−0·05	+0·05	+0·89	+0·14	−0·44	−0·78	−0·06	+0·01	+0·24	+0·14
VIII	+0·35	—	+0·67	—	+0·41	—	+0·51	—	+0·37	—	−0·06	—	+0·29	—

* Pre: pre-operational scores compared with norms of temporal lobectomy cases before the operation.
† Post: post-operational scores compared with norms of temporal lobectomy cases after the operation.

scores. This pattern is comparable with the findings obtained on the dominant temporal lobectomy cases after the operation (Meyer and Jones, 1957). Also, as expected, the differences in the general intellectual level for each patient before and after the operation are not large enough to confirm a real change in the intellectual status.

Table III presents "Z" scores on the learning tests. These scores were calculated using means and standard deviations of the respective dominant and non-dominant temporal lobe groups obtained from a previous study of epileptic patients without massive lesions submitted to temporal lobectomy and studied both pre- and post-operatively (Meyer, 1959).

As expected, the non-dominant cases in the present study do not deviate significantly on any of the tests either pre- or post-operatively from the means of the non-dominant temporal lobe epileptic group. Thus massive lesions of the non-dominant temporal lobe, like anterior temporal lobectomy of the non-dominant hemisphere, have no depressing effect on auditory, visual, or tactile learning.

Consistent with our expectations, most of the dominant cases before operation manifested a considerable impairment of auditory learning ability but not of visual or tactile learning, the scores for which remain comparable with our controls. In Cases I, II, III and IV the pre-operative assessments with the three auditory verbal tests (N.W.L.T., A.V.R., A.V.Rg.) mostly lie outside the pre-operative distributions of the control group of dominant temporal lobe epileptics. Only on A.V.Rg. do scores of Cases II and IV fall within the range of normal deviations, and even then their scores are high and in the expected direction of deficit. After operation there was no improvement in auditory learning in Cases I and III which again was to be expected as the pathological nature of the lesions did not allow of recovery of the damaged portions of the temporal lobes. In Cases II and IV, however, clinical recovery occurred as a result of operating, and in both cases considerable improvements on all the auditory learning tests were recorded so that their scores came to be within the pre-operative distributions of the normative data. The two scores of these two patients, therefore, show striking improvements, and these improvements are probably due to restoration of normal temporal lobe function consequent upon successful therapy without excision of any part of the temporal lobe.

Case V differs from the other members of the dominant temporal lobe group in that both before and after operation the expected auditory learning deficit was not seen. His auditory learning ability is apparently poorer than his visual and tactile learning, but his scores on tests of auditory learning are within the distributions of the pre-operational temporal lobectomy cases. The likely explanation for this is to be found in the site and nature of the tumour. The tumour was purely intra-ventricular and merely expanded the temporal horn. It did not invade or invaginate the cortex of the temporal lobe or such structures as the uncus and amygdala in the way that the other tumours did. It produced epilepsy, but apart from this probably did not disturb the functioning of the temporal lobe as did the other tumours. We have included this case in our series, however, because of its size and unusual nature, and also as a warning lest we become too dogmatic.

SUMMARY

Effects of massive lesions of the temporal lobe on certain cognitive functions have been reported. These effects are comparable to those, previously reported,

resulting from the anterior temporal lobectomy for temporal lobe epilepsy. Massive lesions of the dominant temporal lobe can lead to a specific impairment of auditory verbal learning. After successful therapy the impairment may disappear, suggesting that normal temporal lobe functioning has been restored. There is no specific impairment of either auditory, visual or tactile learning abilities with comparable massive lesions of the non-dominant temporal lobe.

ACKNOWLEDGMENT

This investigation has been supported by a grant made to one of us (V.M.) by the Board of Governors of the Bethlem Royal Hospital and the Maudsley Hospital.

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NORMAL AND ABNORMAL DEPERSONALIZATION

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THIS paper is offered as a contribution to the better understanding of depersonalization. It is divided into two sections. In the first section an account is given of the occurrence of brief episodes of depersonalization in young normal adults. In the second section a consistent interpretation of the symptoms of the syndrome itself is attempted. The two sections are loosely connected; the conclusion drawn from the study of the material in the first section—that it is the persistence, and not the nature of depersonalization which is abnormal—needs to be applied to the considerations advanced in the second. The interpretation will do as well for the brief experiences as for the established syndrome. The writer hopes that—if the interpretation is acceptable—the way will be cleared for attention to the remaining problem posed by this perplexing condition; why, in some cases, it endures. The following abbreviations are used throughout: For the depersonalization syndrome DP; for the depersonalization symptom, *dp*; for derealization, *dr*; for desomatization, *ds*; for the loss of feeling which frequently accompanies the other symptoms, *dE*; for visualization, *vs*, and for loss of visualization, *dv*; for the slowing-up of subjective time, *dT*.

I

i. Three groups of students (N, K and P) were examined for the existence of, or proneness to, brief episodes of DP. The examination was by questionnaire. The questionnaire was headed by a brief summary of the main symptoms of DP (*dr*, *dp*, *dT* and *dE*). It contained the following questions:

1. In the summary of symptoms printed above, indicate by X those which you have experienced.
2. State the duration of your episode or episodes of depersonalization.
3. State their frequency.
4. State any condition, such as fatigue, danger or nervousness, which is constant in your experiences and which may help to determine them.
5. Write a full account of one such experience and attach it to this questionnaire.
6. If you have never had symptoms such as those outlined above, write "No" here.

Name................................ Age........

Before they considered the questionnaire each group was addressed by the writer, who for about forty minutes described the main symptoms of DP as clearly and as vividly as he could. No attempt was made to discuss theories of causation, and methods of treatment were only briefly mentioned. The students were then taken through the questions. Two groups were asked to complete the questionnaire in the following twenty-four hours. The third group (P) completed theirs on the spot; these supplied the highest proportion of positive answers. It was made clear that question five was regarded as the most important one. The students were asked, when answering this question, not to be too critical of their experiences, but to put down any episode which approximated to DP; analysis and acceptance or rejection to be left to the examiner. They were asked also not to ignore the questionnaire if they could describe no such experiences. It was made clear that negative replies were as important as positive, since they gave some idea of the proportion of positives. It is unlikely that all students in the groups N and K returned their questionnaires. It was felt, however, that the replies probably reflected reasonably accurately the proportion of positive to negative in those addressed. The name of the student was not insisted on, but all were asked to make clear their age and sex. Groups N and P were psychology students, group K consisted of philosophy students. There were more "doubtful positive" answers from group K than from N or P.

ii. Fifty-nine replies were received; two were set aside by reason of age, for inclusion in an older comparative group. The positive answers in the remaining number were then examined. Their acceptance or rejection clearly depended upon a reading of the descriptions given in answer to question five. Assessment of these had to be subjective. The "method" used was to assume or imagine in each case that an account written by a depersonalized person was being read, then to decide if the account were true to life. In effect, each account was matched against the examiner's knowledge of the phenomena of DP, drawn from his memory of patients' descriptions of their symptoms and of descriptions in the literature. The assessment produced these results:

	N	K	P	Total
True positive	5	7	11	23
False positive	2	8	6	16
Negative	7	7	4	18

iii. (*a*) Sex distribution: Of the total of 57 students who replied, 33 were female, 24 male; in two cases the sex of the student was not clear. Among the true positives, 18 were female, 5 male and one unknown. Among the false positives, 5 were female and 11 male. Among the negatives, 9 were female, 8 male and one unknown. The percentage of women in the sample was $57 \cdot 9 \pm 6 \cdot 5$, and in the true positives was $75 \cdot 00 \pm 8 \cdot 83$. The difference ($17 \cdot 1 \pm 11 \cdot 0$) is not significant. Mayer-Gross (1935) and Shorvon (1946) describe a more emphatic preponderance of women in their series of cases of the DP syndrome. (See also paragraph vi, infra.)

(*b*) Age-distribution: The mean age of the sample was $21 \cdot 19 \pm 3 \cdot 5$ years, and of the true positives was $21 \cdot 35 \pm 3 \cdot 06$ years.

(*c*) Distribution of symptoms: 19 true positives had *dp*, 14 had *dr*, 10 had *dE*, 5 had *dT*, 1 had *dv*, and 1 had *ds*. *Dp* alone was mentioned by four positives, and *dr* alone by four. One student reporting episodes of *dp* and *dr*, said they never occurred together. Another witness, reporting *dp*, *dr* and *ds*, said that most of her experiences were of pure *ds*. No other symptom occurred unaccompanied.

(*d*) Frequency of experiences: Replies under this heading were so variable that it is difficult to summarize them. Four recorded single episodes, and three of these were at some distance in the past—3 years, 7 years and 11 years previously. Of the rest seven students reported their experiences either as events in past, or as events of diminishing frequency. Twelve replies indicated that the experiences were current possibilities, but of these only one stated that they were increasing in frequency. Eleven students reported frequencies of once or more a year, and of these six described attacks occurring more than once a month. Six students described attacks less frequent than one a year. Five gave answers too imprecise to list in this way.

(*e*) Onset and duration of experiences: Eleven students noted the age of the first episode. These were 4, 7, 12, 12, 12, 15, 15, 15, 17, 17, and 19 years. The mode of onset was discovered from the descriptions, and findings under this head depend upon the assumption that in this regard a student's description of one attack is typical of all attacks experienced by him or her. In ten descriptions the mode of onset is not mentioned. In ten descriptions the onset was sudden, and the word "suddenly" is used to introduce the experience; in two it was rapid, and in one gradual. This may be compared with Shorvon's case-histories of 66 patients, of whom 61 described a sudden onset (*ibid.*). In duration, the experiences of different students varied between momentary duration and a span of two days. Students having a number of experiences tended to have them for the same length of time. The mean duration was calculated as a grand mean, the assumption being made that each positive had an equal number of attacks; the figure was 5 hours 13·75 minutes ±3 hours 44 minutes.

(*f*) Associated conditions: Answers to Q.4 fall into three groups. In the first group no condition is significantly or constantly associated with the attacks. There were three of these, and in two others the conditions mentioned —"vague sense of emotional disturbance" and "slight fatigue and nervous strain"—appeared to have little relevance. In the second group of two answers the conditions cited were those of background states, anxiety and frustration, which appeared not to be directly connected with the attacks. In the third group of seventeen answers the associated experience was emphatic and its connection with the attack direct. Ten of these mentioned fatigue, usually in association with other conditions such as nervousness, danger, menstruation, high room-temperature, novel surroundings, convalescence. The remaining answers did not group together; they included excited expectancy, relief after tension, after being in company, nervousness, and exhaustion during a dangerous illness. Fatigue therefore is by far the commonest factor in these DP experiences, as judged by the answers to Q.4. A somewhat different impression is made by the answers to Q.5, which in all but one case mention the setting of the experience described. In twelve out of twenty-three descriptions it is plain that the describer had recently passed through a period of effort, danger, strain or mental concentration. In three, the experience was one of illness, in two of grave illness—and in both these DP developed at the time when the student entered hospital and her illness became the active concern of others. In one case the experience cited was one of personal danger; DP developed half an hour later. In these instances there is a similarity of experience between the students and patients who develop the "Calamity syndrome" (which includes DP) described by Roth (1959). Five mention recent concentrated work at or for examinations; in each of these the work was in the recent past, and

DP occurred in the time of reaction after it. While it is plain that at the time of DP many of the students were tired, it is unlikely that fatigue was a causal factor; it seems rather that DP developed in circumstances of reaction when fatigue makes itself felt. If one can generalize from the descriptions above, it seems that DP does not develop—or at any rate did not develop in these normals—during activity, but usually after excessive activity or emotional engagement.

iv. *Examples of "true positive" descriptions:*

(*a*) "I was very tired after a hard term and had been working intensively for several days. I felt unwell and apathetic. Sitting in the Refectory at lunch time one day, I suddenly felt as if I was completely detached from my surroundings. I was still in a way conscious of the fact that they were still there, but somehow they did not seem tangible. Although I realized where I was, I felt in no way part of the situation. In some way I had lost contact.

"I was able to talk to the people around me, but it was only with great effort that I could keep up interest in a conversation. All the time I seemed to be drifting away, and it was only with conscious effort that I could concentrate.

"After lunch I went for a walk in the woods. It is very peaceful and restful there, and after an hour or so I gradually began to relax and the detached feeling passed off slowly. In the evening I was able to concentrate on my work again." (K42; female; 20 years.)

(*b*) "The most usual occasion when this occurs is when I am out of doors. The last time was within the last month or so. I was in Nottingham with a friend and suddenly as we were walking along, I seemed to be completely apart from myself. I felt that I was somewhere above looking down on the scene of which I was a part and yet not a part. I was walking and talking, as though automatically, I couldn't feel any movement and yet I knew that I was walking.

"Everything appeared to be of little importance any more, and yet all the time I wanted to get back and be completely whole once more. The experience on this occasion lasted for at least five minutes, but time as far as I remember passed as usual. We crossed the road, and although my legs moved with the motion, I felt that my brain had gone somewhere else and from there was just watching me.

"I was completely unable to tell whether I myself was still present or whether I was the part which had gone. In short there were two different beings, the one watching the other.

"The experience disappeared as suddenly as it had come and once again I felt complete." (P91; female; 19 years.)

(*c*) "Mild flattening of awareness of self, external objects and emotions always accompany prolonged physical fatigue. But an intense feeling of desomatization of all the body except the head occasionally occurs as part of a short depressive episode. There is a feeling of extreme fatigue, and an inability to cope with or be interested in persons or things—coupled with emotional distress at this inability. I usually go to bed and give up all attempt at physical activity, and as soon as I relax I get an intense feeling of 'ME' being located in my brain just behind my eyes. I am extremely aware of myself as being alive and existing in this particular place, but the rest of my head and body—except my eyes—does not belong to 'ME'. My body is felt as a pure biological machine automatically pumping food and air to keep alive my brain. I feel detached from my body except through a few channels somewhere and that it could be removed and another 'screwed on' without in any way affecting my essential personality. This feeling usually lasts about an hour and is coupled with depressive thoughts on the hopelessness of attempting to cope with life, etc. I usually then fall asleep and 2–3 hours' sound sleep is enough completely to remove all these symptoms." (P101; female; 25 years.)

(*d*) "The first experience was the most vivid probably because accompanied by terrible fear on account of the uniqueness. At some period after this I learned that my mother had had similar experiences, especially when young, and I therefore regarded the rest as quite normal and this helped me to throw them off more quickly.

"The first occasion was a sudden onset as I entered a room in a strange house (I am not sure whether I had been there before but certainly not often). For some minutes I was alone in the room and I had the impression that had someone come in I should have been unable to make an immediate response but my actions would have been delayed as in a case of absent-mindedness.

"I stood in the middle of the room and looked around—this seemed necessary because the objects had become not only unfamiliar, in the normal sense, but also unreal, in the sense that I had to tell myself what their use was, in the way one might describe it to a foreigner.

"This took place as an internal monologue with hardly any pictorial imagination, whereas normally I do much concrete thinking in pictures accompanied by vocally imagined sounds.

"My impression was that I did this to reassure myself—bring myself back. The most striking feeling being that I did not know what a person was. In other words I was saying to myself, 'I am a human being and my name is S— N—, but whereas this would normally have been a joke or a tautology because I could not imagine being anything else, it here took on significance because having a feeling of strangeness—that is, that it could be questioned.

"I was aware of exactly what I must do in order to appear normal but this was now a conscious effort and was more like manoeuvring a puppet.

"I do not find these experiences connected with fatigue, etc., because I find that to a certain extent this feeling can be induced or, at least, encouraged and also that I can force myself back to normality by concentrating on some other interest. I do not think I should find this so easy if I had not got over the fear which this first experience induced." (K23; female; 21 years.)

(*e*) "Feeling that surroundings are unreal and I am apart from them. They go flatter and fainter. Attacks don't last long and I feel perfectly all right before and after." (P105; female; 19 years.)

(*f*) "This experience of depersonalization occurred to me when I was about twelve years old and on holiday in Devon. I was walking along a road, the first or second day after I had got up after being ill with a stomach upset.

"Everything had seemed quite normal, and then it seemed as if I had become two people. One half of me was watching the other perform in a completely disinterested way. I could hear my voice and that of other people's very remotely, although there was no lessening of sound. It seemed rather pointless to reply to remarks made, but I heard my voice doing so. Time did seem to be going much more slowly—this I noticed mainly in relation to the voices I heard.

"I felt that no action I did had any particular relevance. The thought occurred to me that if I had had the energy I could have jumped over a cliff, and it would not have mattered at all. I did everything, walking, talking or listening with complete lack of emotion, for it was not me who was performing these actions, but another person who seemed somehow to be in my body. There was no link between this part of myself and the self that was standing outside watching the actions.

"I cannot remember any derealization in my perception of the external world, except as I have said that the voices I heard seemed remote, as if coming from a wireless set rather than from real people with whom I was intimately connected.

"I find it difficult to recall the duration of the time; it may quite possibly have lasted ten minutes or for forty or so minutes, because time had no relevance at all. There was no gradual coming back into a normal state of feeling. Suddenly I was no longer two people, but one again; the world seemed relevant, and I possessed my own personality." (P90; female; 23 years.)

v. *Examples of rejected descriptions:* Some very discursive "false positive" answers were returned to Q.5, particularly by male students in Group K. Two brief examples are:

(*a*) "I have felt these symptoms when walking alone after an evening in a 'pub'. As a result of these conditions it is difficult to isolate a particular occasion. In general I have suddenly become aware that I was walking extremely quickly without having intended to do so, and my actions seem directed by something other than my conscious personality. I observe them as something unconnected with myself, and when I have seen, for example, that my hand was about to strike a tree or wall have done nothing to prevent it. In this state though my mind seems to be working rapidly, external stimuli like rain or cold are observed rather than felt. I become aware that my limbs are not properly controlled but I am unable to exert a control over them, even if I wish to do so. How I withdraw from this condition I am not certain, but I believe that I gradually connect my mind and my body, and I feel 'back in myself again'." This answer describes inebriation, not DP. (P92; male; 24 years.)

(*b*) "I have experienced a certain flattening of emotionality generally. I am less able to be moved by music or such sights as a sunset. I find myself faking a feeling which I do not experience in order not to appear lacking in sensibility. I express conventional words of shock when I do not feel in the least shocked.

"Because I do not feel that my presence will alter any situation in which I find myself I have tended to lose interest in many things which formerly did interest me." This condition, present for a period of two years with no other manifestation of DP, appears more probably to indicate incipient schizophrenia. (P106; male; 21 years.)

vi. Comparison with a group of older persons was effected by distributing the questionnaire to a number of psychiatrists. No preliminary lecture was given; it was felt that the responder's own knowledge of DP should suffice. An additional question was inserted after Q.3:

> 4. If they (the episodes of DP) were more frequent at an earlier age, give the time-span of their maximum frequency.

Thirty-five replies were received, to which the two replies mentioned in paragraph (ii) were added. Thirteen described valid experiences of DP. The proportion of positives comes pretty close to that in the group of students.

The mean age of the group is 39·51 ± 8·64 years; of the negative responders, 40·41 ± 9·15 years; of the positive responders, 37·84 ± 7·9 years. Six of the positives (mean age 33·1 years) described their experiences as current events; seven (42·0 years) placed them in the past. Six women and thirty men replied to the questionnaire; in one case no conclusion could be drawn as to the sex of the replier. Two women gave positive replies. Thus, a predominantly male sample produced a proportion of positives not much below that of the students, of whom 33 out of 57 were women. With three exceptions—one, who recorded an experience at the age of 7, one who recorded present liability to DP at the age of 42, and one a similar liability at 39, the experiences occurred in an age-band extending from the onset of puberty to the 36th year. In other words: those having present episodes of DP are, with two exceptions, under thirty-five.

vii. *Commentary:* Out of a sample of fifty-seven young persons, twenty-three show a past or present liability to brief episodes of DP. These were selected by the tester on the basis of their descriptions of a typical episode. Selection had to be subjective, and this introduced a possible source of error. To minimize such error the descriptions were read, and the selection of true positives made, by a colleague L.W.B. He found twenty-seven positives. With one exception, all the writer's choices appeared on L.W.B.'s list, which contained five answers not on the writer's. The conclusion can be drawn with some safety that more than a third of the students examined described valid instances of DP. The DP syndrome itself often begins with a run of brief episodes. But from the numerical standpoint alone it is highly unlikely that the students, or a number of them, were exhibiting the prodromal stages of illness. The sample, more probably, contained a large number of individuals who although normal and healthy are briefly subject to DP. The sample is a specialized one. It is distinctive in age, occupation and intelligence. It possibly contains a higher proportion of unstable persons than the universe of persons of the same range of ages. It is a suggestible group, which may have been influenced by the oral and printed descriptions of DP when completing the questionnaire. It is not large, and the proportion in it of true positives (40·35 ± 6·63 per cent.) carries a considerable standard error. All these features of the sample have to be weighed when considering what inferences can be drawn from the test. It is fairly clear that brief, repetitive DP cannot occur in the general population as frequently as it does in the sample. If it did so its existence would have been recognized and its incidence acknowledged in the literature, in which there is reference to descriptions of DP by exceptionally gifted individuals (e.g. Mayer-Gross, *ibid.*), but no comment as to whether these were normal or morbid experiences. It may be that these descriptions come from the same kind or universe of persons as those tested, and that brief DP as a normal experience does occur in a proportion of young, intelligent and reflective individuals. No valid inference can be drawn from the test as to its occurrence in the general population; but it can at least be said that DP can occur in two ways—as a persisting state, and as a brief and often repetitive state; the latter may herald the former, but more frequently does not. It can also be stated that persons subject to brief unominous DP probably far outnumber those who develop persistent primary DP. These comments are not disturbed by the results of testing an older group of persons. The enlarged sample (94) has a proportion of positives of 38·3 ± 5·01 per cent. There is confirmation of the statement that the brief episodes described do not run on into prolonged DP. An upper age-limit of about thirty-five is set to the propensity to have the episodes. No tendency to favour one sex rather than the other is observed. All the persons tested are, or have been, university students; there is no conclusive evidence, however, that undergraduate life itself is a factor in the production of episodes. There is a suggestion (not statistically confirmed) of three periods of propensity in the age-band of incidence—one in puberty and early adolescence, one in the late teens and early twenties, and one from twenty-five to thirty-five.

II

INTERPRETATION

i. In the following account *dr*, *dp* and *dE* are dealt with in that order and in most detail; some consideration is then given to *dv* and *dt* and to "as-ifness", the metaphorical phrasing of symptoms. The section concludes with a short note on the patchy distribution of symptoms, and a summary.

The interpretation starts from the propositions that *dr*, the most unambiguous occurrence in DP, does not differ in kind from *dp* and *ds*; that *dv* gives a clue to what happens in *dr*; and that *dE* is a result of what happens in *dr*. Since *dr* is clearly a disorder of perception, it implies that *dp* is also a disorder of perception, and that *dE* results from a disorder of perception. The nature of the perceptual loss in *dr* is first to be defined. This will be more easily done after a survey of the development of perception, since what is lost in *dr* is believed to be an element which is added to perception as it matures. The course of development as traced here is theoretical and speculative; its authority derives chiefly from its fitness to explain *dr* and perhaps other perceptual anomalies. Its understanding will be facilitated by a preliminary statement of the scope of imagination. Though a great deal has been written about images and imagery, not much has been written about the power of voluntarily producing images. One of the few to approach it as the subject of psychological study—Sartre (1948)—has stressed its importance as a constituent of consciousness. "Ainsi l'imagination, loin d'apparaître comme une caractéristique de fait de la conscience, s'est dévoilée comme une condition essentielle et transcendantale de la conscience." In the author's view, it takes part also in an intimate and essential way in the evolution of perception.

The immobile imaginer can summon up images around him, or be spontaneously visited by them, in the present time. He can also without movement represent himself as another person or object; and thus in part transform himself into an image. He can in part, and at once, represent or reconstitute himself among images of distant scenes and at different times from the present. He can in part reconstitute himself at another point in an observed scene, changing its pattern and resolving it into an image, and he can represent himself as another person or object at this point, in both instances transforming himself in part into an image. These exercises of the imaginer result in sensory and emotional experiences which are partially satisfying. Realism and vividness are sacrificed to a greater or lesser degree. They are rarely sufficient to extinguish current perceptions. Nor do the representations of himself obliterate his sense of his own identity, though each diminishes it.

ii. The infant has no external world. He is aware of sensations which are produced or aroused by objects. These sensations are the only representations of objects which he knows; his representations of objects are therefore completely internalized. Later, in that important developmental era, the third quarter of the first year, awareness of the parts of the body, the first object to be explored, is achieved. With this knowledge, though slightly later and perhaps to a lesser degree, the existence of objects other than the body is realized. These objects combine with a series of internal sensations which are recognized by the perceiver. He interprets his discovery of objects by means of a belief that they have passed from inside to outside his body, and their association with internal sensations means (for him) that they are still parts of him. He learns more objects by clutching and mouthing them, applying to them the same process of absorption and ejection which appears to him to have been undergone by his primary objects. This enables him the more readily to regard his new objects as parts of him. At the same time that he acquires objects, he learns space, by crawling, climbing and tumbling. He also learns to "place" his objects in a spatial setting. But since the only space he knows is that into which he has taken his own body, the cognition of space does not at first affect his belief that his objects are parts of him. Space, at this stage, carries a strong personal sign.

iii. This second stage of perception cannot be of long duration. The experiences of the maturing infant must bring strong pressure to bear upon the belief that his objects are part of him. He must soon become aware that a number of "parts of him" at times remain stationary when he is mobile, or at times move when he is stationary in directions which he does not control. The increasing profusion of objects further embarrasses his primary assumption. His own space—the area in which he moves—becomes extended; and by exercising his power of visual accommodation, already trained by the focusing of objects in that area, he is able to place objects at increasing distances from him, and increasingly far away from his own spatial orbit. These distant objects cannot be accommodated by the simple belief that all objects are parts of him. He then substitutes for the statement "these objects are parts of me" the statement "these objects are as if parts of me"; not "like parts of me" merely. This involves an important change in his attitude to objects. Whereas they are first simply parts of him, they are now imagined parts of him, and this imagination calls for the conscious representation or reconstitution of himself in each object. He in part transforms himself into an image which occupies the boundaries of the object, and in so doing suffers some diminution of his own sense of identity. Such an exercise falls easily within the powers of the imagining child. At first conscious, it becomes increasingly effortless, until at mature perception it forms an important element of subconscious perceptual adjustment, and the diminution of the perceiver's own sense of identity is reduced to zero. In addition to the renunciation of objects as parts of himself, the developing perceiver renounces space as the content of a perimeter which is believed to be a vague outer margin of his body. For that space which is learned, and attached to him, by his own journeys, he substitutes distances covered by representing himself in part in imagery, at their end-points. This conscious reconstitution of himself in the perception of distance also becomes subconscious and automatized in development.

iv. If the mature perceiver should suffer the loss of this particular perceptual adjustment, there will be impairment of attachment, realism and 3-dimensionality. The adjustment is effected in order to retain as far as possible the feeling that objects are parts of the perceiver; its loss must produce a sense of separation from them, and a sense that they have become extruded from his personal world. Furthermore since the adjustment consists of an imaginative reconstitution of the perceiver in the percept, its absence will set a bar to "going into" percepts, and these will stand off from the perceiver in a strange and hitherto unexperienced way. Again: the purpose in the retention of the feeling that objects are parts of the perceiver is to maintain a common standard of realism. If objects are such, they are at least as real as the body; the adjustment sustains the realism of the scene. In its absence, objects will appear to be both unreal and remote. Since space is subconsciously constituted by the same component of perception, deletion of the latter will gravely affect the assessment of distance and perspective. Impairment of spatial perception must in turn affect the apprehension of solid objects. Large objects are apprehended by a refined application of the methods used to decipher space, in particular by the inference drawn from the exercise of visual accommodation. They are construed in the same way as space is construed. The solidity of small objects is realized by descrying in them the same visual patterns *in petto* which are associated with solid large objects. When large objects appear flat, the presence of similar visual patterns on small objects will fail to carry its former conviction of their solidity.

There is an obvious and close similarity between these effects and the condition of *dr*. One may conclude that, if the author's account of perceptual development is accurate, it provides for the absorption into perception of a process whose contribution changes derealized to normal perception. Without it, perception fails in realism and attachment and the perceptual and physical worlds approximate more closely (Brain, 1951).

v. It is further assumed by the writer that the change in experience which produces *dr* is identical with that which produces *dp*. This assumption would from inspection appear to be correct. In each case the effect produced is one of strangeness. The depersonalized person is a stranger to himself—often describing his state in that precise way. The derealized person finds the world strange because different from any previous perceptual experience of it; and this strangeness invests equally perception of fresh and familiar objects. In each case there is an effect of remoteness and detachment. The depersonalized person describes himself as a spectator of his own actions. The derealized person watches objects, scenes and events as though they were the traffic of a play—an illusion heightened, but not mainly determined by the two-dimensional quality of his vision. In each case there is loss of realism in the thing perceived. In each case there is loss of substance in the thing perceived; in *dp* the observed self disappears or becomes shadowy, in *dr* objects become flat and weightless. In each case a sort of fission is described. In *dp* the sufferer is separate from, and in search of, his own self (*alter ego*). In *dr* there is a fissure between the patient and the world—an absence of that integration with objects which he formerly possessed, albeit without conscious awareness of it. It may be remarked here that the author's emphasis on detachment brings him pretty close to Ackner (1954), who ascribes the symptoms of *dr* to non-integrated experience.

The change of experience in *dr* appears to be the loss of the self-representing component from perception. If *dp* is also the result of a similar impairment of perception, what is the percept?

vi. At the core of all experience is the very self, the imaginer. The imaginer cannot be an object to the individual, for to be so he has to be made into an introspective image which only he can supply. The imaginer continually retreats before introspection. He can be an object only to an outside observer. But the individual has an early and pressing need to apprehend himself, and to do so he creates a self-image. In this the body is utilized, but it is a percept of a different order from the body as an object. It is a construction—like other percepts—in which the individual represents himself within an object, in this case the body. But here he creates or objectifies himself—not his body or his other objects of attention. The self-image is set up soon after the development of self-awareness. It is not essential to this, though it may facilitate it. It is not present —or need not be present—in the second stage of perception, when objects though outside the body are believed to be parts or pieces of the body. When the existence of independent objects is conceded, the body is defined as well as the objects outside it. Self-awareness comes with knowledge of the body. With self-awareness comes the ability in imagination to pass into the body and outside the body. Thus are set up the conditions by which the imaginer, the aware self, can apprehend himself by the development of a self-image; can perceive his body as an object; and can enrich his perception of objects by representing himself in them. The self-image, therefore, arises early in the third stage of perception.

vii. It is the deep percept of the self-image which is affected in *dp*; the latter, indeed, consists of loss of the self-image. There is a failure by the imaginer to utilize bodily clues to set up or exteriorize an image of himself. In *ds* he is unable to objectify the body, or parts of the body, by failure on a more superficial level to represent himself in it. In *dr* there is a localized or partial weakness of imaginative power which renders the observer unable to represent himself in objects. In *dp* the individual returns to—and stays in—the brief primitive developmental period of self-awareness before self-apprehension. The object of normal introspection is lost; the individual becomes an object only to an outside observer. It is not difficult to understand that abnormal, intense and fruitless introspection will ensue: an unavailing search for the self-image, the persistent scanning of a blank internal environment.

There is a difference of a kind between *dp* and *dr*. In the former the object or percept as a whole is lost, in the latter a component of perception is lost. The component is one of self-representation in the percept; the object is a representation of the self. Loss of the self-representing power or process is bound to crumble and efface the self-image; the two effects are truly identical, though they occur over different areas of perception. What is the relation of the body-object, in *dp*, to the world of objects, in *dr*, when both have lost the representation of the self? There is a difference between them. In *dp* there is no recognizable object—no "self"; in *dr* the objects are present, but their perception is attenuated. (The body is not a form of the self-object.) In *dp* the body loses its property of belonging to the perceiver; it is disowned, but not (in the absence of *ds*) derealized. Since the individual can no longer "place" himself in his body, the latter will seem to behave as a selfless automaton. Since he is in a new and special sense apart from his body, he will watch it like a spectator.

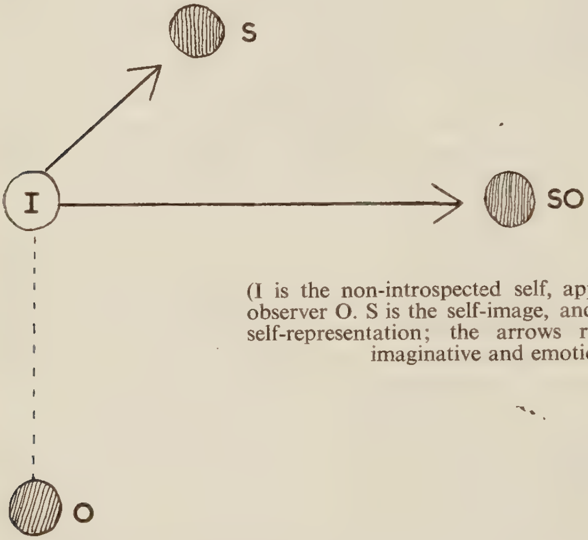
viii. DE is a by-product rather than a direct effect of DP. It develops together with the derealization of objects of all kinds. It is not an inevitable outcome of *dp*, despite the intense involvement of the individual in his emotions; though, as will be shown later, the attenuation of the self-object may aid its development. Objectless emotion is not affected by *dE*; it is objective emotions

—sentiments—which fail. If, as the writer believes, the loss is to be construed as an inevitable outcome of *dr*, then in the severity of its effect *dr* is more akin to imperception, where the lost object is no longer recognized, than to removal of the object from perception by death or absence. In instinctual psychology acts of perception are described as the initiators of specific instinctive feelings and actions. It is nevertheless stressed, in most accounts of the psychology of perception, that emotion enters deeply into, and much affects, perception. It is also stated, for example by McCurdy, that lack of emotion diminishes the sharpness and realism of perceptions—produces *dr*, in fact. "When we have emotional contact with anything"—(he writes)—"we are identifying ourselves with it. When this identification takes place the thing feels 'real'; before that, it is phantasmal, shadowy" (1925). The author suggests that it would be better to preserve the distinction between, and relative independence of, perception and emotion—the one a mental operation, the other a mental state. It would be better, and truer, to say that the full use of perception permits the development of appropriate emotion than that emotion in some way combines with perception in order to sharpen or alter it. It is true that in anxious expectancy there is quickening and (maybe) apparent distortion of perception. But though this leads to restriction of the field of attention, and sometimes to premature breaking-off of perception, and in such an indirect way exerts an effect, it does not, strictly speaking, affect the process itself. Furthermore, the anxiety is a result of previous perceptions.

"Emotion" is a substantive derived from many adjectives used to denote a state of mind. It does not exist as an entity, any more than a word coined from the adjectives used to describe states of matter would label an entity. A particular emotion is said to be present as and when the mind alters its state, and to persist until this state alters. If the mind alters its state upon perception of an object, sentimental emotion is said to exist. A two-way traffic is felt to be present in such a case. The object is said to evoke feeling in the perceiver, and feeling is considered to flow towards or into the object. It is this sense of flow to the object which has probably led to the belief that emotion directly affects perception. The author now suggests that (if his account of perceptual development is correct) sentimental emotion must necessarily depend upon the presence in the percept of a representation of the observer. Or, in other words, that in *dr*, where this component of perception is lacking, sentimental emotion must fail.

Self-representation in objects completes perception in two ways. It binds the object to the perceiver, and it puts the object on the same level of realism as his own. A third effect should now be noted. Though the intention—and the effect—of the operation is to transfer himself into the object, in imagination to surround or clothe himself with the object, in a sense to be the object, the observer is also, by means of the objects, setting up a number of implicit and largely unacknowledged self-objects. These are not at the same level of awareness as the one self-image, nor do they diminish the reality of the self-image. But they are nevertheless representations of the self which because of their setting become objects of attention by the (non-introspected) self.

Turning now to the process of acquisition of emotional objects—that is, to the increasing number of changes of mental state which follow perception; the infant at first fills up and spills over with impersonal rage or pleasure. With self-awareness these feelings become personal: "these feelings are mine". With self-apprehension the first object of emotion is acquired; the infant loves or hates himself. With the acquisition of physical objects comes the capacity to harbour feelings by and for objects. But these contain, or come to contain, representations of the self. May it not be that these arouse emotion because of this? That the strong emotions directed upon the first object, the self-image, can now be directed on similar representations in outside objects because of their close relationship with it? If this is so, it is the self-in-object which receives, is the real object of objective emotion. All sentimental states exist because of the re-duplication of self-representations. Altruistic emotion depends upon the degree to which the imaginer unites with—or identifies with—the object. Such a theory does not account for the difference between objects in the power to arouse emotion. But it does seem to show that perception completed in this particular way may be necessary before emotion can develop.



(I is the non-introspected self, apprehended only by an outside observer O. S is the self-image, and SO the object completed by self-representation; the arrows represent the routes both of imaginative and emotional transference.)

When feeling is aroused by, but not directed upon, the object there is a relationship with, and perhaps a return to, infantile pre-personal pleasure.

ix. Thus, in *dr*, the perceiver can be said to have no self-in-objects, and therefore no emotional objects. All objects assume the condition of those objects whose full perception is normally not associated with feeling. All will be emotionally neutral. Perception will lose its emotional after-effect. Feelings in the self will occur, but without perceptual evocation. The individual will return to the infantile state of undirected emotions. These will be personal only in so far as the experiencer escapes *dp*, and retains his self-image. If the ability to construct this is also impaired, he will find it difficult to acknowledge his feelings as his own; this will increase his complaints of loss of feeling. If no self-image exists, there will be no model to accommodate the feeling-tones which accompany actions. Feeling "by" objects will not be possible when the link attaching perceiver to percept is severed.

x. This concludes the interpretative account of those symptoms of DP which it is most important to interpret correctly—*dr*, *dp* and *dE*. The section is brought to a close by notes upon *dv* and *dT*, and some consideration of the two features of DP which affect its symptoms as a whole: "as-ifness", the qualified phrasing of patients' descriptions, and the patchy exhibition of symptoms in the individual case (Lewis, 1935).

xi. *Dv* could well be expected from the nature of the perceptual failure, as this has been outlined above. If there is a failure to reproduce imaginatively the self in objects, there might well be also a failure of the imaginative capacity to succeed in visualizing. It is not clear, however, why *dv* occurs only in some cases of DP, and not in others. Nor can *dv* be causally related to *dr*. When *vs* is lost as a result of lesions affecting Brodmann's area 19 (Brain, 1957) there is no record of *dr*-like experiences resulting. Also the occasional loss of *vs* in *dr* appears to contradict the Jacksonian rule of the order of dissolution of functions in the central nervous system after a physical lesion (*Selected Writings*, 1931): here, the more voluntary and less organized function of *vs* disappears later and less frequently than the less voluntary, more automatic and more specialized function of self-representative completion of perception. *Dv* may be regarded as a clue to the kind of perceptive inhibition that occurs in, and produces *dr*, but its exact relationship to *dr* is not known.

xii. The slow subjective time of DP is, in the author's view, a basic slow time which is uncovered or released by *dr*. In individual development it comes to be approximated to clock-time under conditions of increasing use of, and familiarity with the latter. Clock-time is learned by frequent perceptions of the clock-face combined with a knowledge of numbers. In *dv* the personal perceptual link to the clock-face is severed, and with it the attachment of clock-time to personal time. The latter then reverts to its original speed. The phenomenon may be compared with the late disappearance and readily stimulated reappearance of the slow delta rhythm in EEG records from the pre-frontal area of the brain (Hill, 1950). The sense of time's slowness leads to paradoxical complaints, as noted by Lewis (1932). The same patient will say that time seems endless (because he cannot reach the future), and that there is no time (because his present appears prolonged). Or a patient may report that a point in the recent past seems ages ago, and also express surprise that clock-time is not earlier than it is. This paradox is to be explained by a difference in the direction of attention. The recent past becomes remote because a short journey has taken a long time. The clock-time seems advanced when attention turns to the slow passing of the minutes. *Dv* probably contributes to the inability of the derealized person to look forward.

In regard to memory: in the early case memories are strong and vivid, being largely drawn from the pre-morbid era. In the long-established case they are poor because for the most part they belong to the era of dulled perceptions.

xiii. Patients' reports of *dp*, *dr*, *ds* and *dT* are frequently introduced by the qualifying phrase "as if". This habit of description is consistent enough to earn the status of another symptom. Patients 'descriptions tend to issue in the form of metaphorical statements. These should not lead the hearer to doubt the authenticity of the symptoms. "As-ifness" has more than one cause. In *dp* there is the difficulty of explaining a perplexing and apparently unique experience—one which the describer believes to be without parallel in the hearer's life. In recent cases of DP the new sensations stand in contrast with former, more vivid, ordinary and more real ones. The contrast leads to their description in terms which question their authenticity. Then, too, there is the fact of insight.

"As-ifness" records the presence of insight, though it is not directly due to insight. It arises in part from the need to emphasize insight.

More important is the observer's standpoint—that of detachment from less real impressions. "As-ifness" stresses the nearness of these impressions to those of reproductions of experience in novels, paintings and photographs. It provides an explicit sign of their apparently reproductive character, though it works in the opposite direction to the "as-ifness" of admitted reproductions. In these, imagined or reproduced experience is implicitly presented as if it were real. In *dr*, actual (though faded) impressions are explicitly described as if they were imaginative reproductions. In *dr* disbelief or doubt is stressed to emphasize insight. In e.g. the novel suspension of disbelief is encouraged. It is a paradox of *dr* that the subtraction of imaginative participation from perceptions approximates these to experiences which are in the main imaginary.

When alteration of time is mentioned it is clock-time, not the new, slow time, which is described illusively. Loss of realism is also described with the prefix "as if"; there is a kind of "squaring" which multiplies the indirectness of the experience: unreality is itself unreal.

SUMMARY

xiv. In perceptual development the non-introspected self (the imaginer) comes to set up a self-image, using the body as a fundament, to form an object of the body, and to complete external perception by representation in objects. These attainments or abilities are impaired in *DP*. In *dr* the impairment of external perception leads to detachment, since objects can no longer be subconsciously regarded as representatives of the perceiver; to lowered realism, because objects are no longer on the same level of perception as the body; and to flatness, because of the incompleteness of spatial perception. In *dp* there is an absence of the self-image. The persistent need to apprehend the self, results in ceaseless and useless self-scrutiny. The body can no longer be used as a basis for self-apprehension: therefore, it is watched by the sufferer as by a spectator, and movements become automatic. In *ds*, self-representation in the body, or in parts of the body, fails, and these are lost as realistic objects. DE appears to depend upon *dr*. The alteration of perception in *dr*, however, depends upon an alteration in the perceiver, from whom the power of representation in objects is withdrawn. This removes the emotional object from objects, which therefore become emotionally neutral; and (looking to the perceiver) reduces or destroys in him the capacity for the development of object-emotion.

The loss of *vs* is the loss of a function on a higher level, in the Jacksonian sense, than that occupied by representation in objects. Slow time is the emergence of basic early subjective time arising from the loss of perceptual attachment to the clock-face, and severance of the link between clock-time and personal time. The metaphorical character of the descriptions of symptoms in DP has three causes: (*a*) the difficulty of communicating an unique experience, (*b*) the memory of more vivid pre-morbid perceptions, and (*c*) the detachment of the observer from less real impressions.

ACKNOWLEDGMENTS

The author's best thanks are due to Dr. W. Mayer-Gross for his advice and criticism, and to numerous psychiatrists in different hospitals, whose information helped to complete the first section of the paper.

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AN INVESTIGATION INTO THE PART PLAYED BY ORGANIC FACTORS IN CHILDHOOD SCHIZOPHRENIA*

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INTRODUCTION

AN investigation into the factors concerned in the etiology and pathogenesis of childhood schizophrenia is fraught with difficulties in numerous areas. Encountered are such problems as the diagnosis itself; doubt that psychoses exist in childhood; the existence of the duality organic or functional schools of thought, and of frequent contradictory findings reported by various groups of investigators in the field.

The present paper is an admittedly incomplete pilot study on a relatively small number of cases of childhood schizophrenia (15) and their non-schizophrenic siblings (33) attempting to reveal certain trends in the histories of schizophrenic cases which point to a field worthy of further investigation. Allowing for limitation of scope, the study appears to indicate the presence of significant difference in these two groups of cases and controls (siblings) as far as prenatal, paranatal, neonatal and childhood "organic insults" are concerned.

Interest in the investigation commenced when the author noticed in case histories of childhood schizophrenia a significant loading as far as these "organic insults" were concerned as compared to their siblings.

The psychodynamic formulations on many types of neurotic childhood disorders seem often to approximate that of cases of psychotic disorder in childhood. Thus, there appear to be additional factors of fundamental importance in the "make-up" of the schizophrenic children—other than the psychological traumata *per se* as exemplified by maternal rejection, lack of protective emotional environment, etc.

As to the existence of the entity childhood schizophrenia, we can best quote Escalona (1):

"Whatever term one decides to use—and childhood psychosis may be taken as an abbreviation for 'grossly atypical development' or for 'severe disintegration of personality', we have an only too vivid mental picture of the type of child to whom these and similar terms are applied."

She continues: "Most of the mothers or other persons in contact with these children spontaneously comment that there is something puzzling and different about these children from an early age on. The mothers never knew 'what to expect'; they lacked the sense of intimacy and close rapport the mothers had known with the other children".

In describing the problem of aetiology she writes: "From experience with non-psychotic children it is well known that behaviour deviations of the kind enumerated (neurotic) are often produced by parental attitudes. Hence, it is easy to assume that in these severely disturbed children, maternal rejection is at the root of the trouble. Yet, the more one studies the early life history of psychotic children, the more is one impressed with the atypical and pathological reaction of the children to perfectly ordinary maternal attitudes and daily routines. The child who rarely provides for the mother the emotional gratification that comes from having the baby respond to her positively cannot help but be upsetting to even the most loving mother. These mothers will 'try everything'—go to extremes in strictness or indulgence. They will seek and receive contradictory advice and act upon much of it, and when we come to take the developmental, inconsistency in management is found."

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* Based on a thesis submitted for the Diploma in Psychiatry of McGill University.

A.—Clinical Diagnosis and Pathogenesis

Concerning exact criteria of diagnosis of the disorder, opinions differ often markedly.

Bender (2) writes concerning her 10-year observation of 100 preadolescent children with the disorder; "a clinical entity occurring before age 11, which reveals pathology in behaviour at every level and in every area of integration or patterning—within the functioning of the central nervous system, vegetative, motor, perceptual, intellectual or social. This behaviour pathology disturbs the pattern of every functioning field in a characteristic way. The pathology cannot therefore be thought of as focal in the architecture of the central nervous system but rather as striking at the substratum of the integrative functioning or biologically patterned behaviour".

She feels the organic disorder engenders pseudo-neurotic, pseudo-psychopathic or pseudo-defective reactions.

"It may otherwise be defined as a form of encephalopathy appearing at different points in the developmental curve interfering with the normal developmental pattern of the biological unit and social personality in a characteristic way and, because of frustration, causing anxiety to which the individual must react according to his own capacities."

A paper in 1953 (3) by Bender and Helme studied their schizophrenic cases comparing them with non-psychotic controls stating: "The theory requires that, even if incidences in given cases do not differ significantly between groups, a given schizophrenic child should tend to show pathology in more areas than does the control." The all-pervasiveness of the disorder was stressed as differentiating it from neurosis where the symptomatology is localized.

Criteria used by the workers at Bellevue read:

(*a*) Vegetative and Motor:

1. Height and weight. Growth problems.
   Vascular lability. (Flushing, perspiring or blue-cold extremities—temperature reaction to slight illness or no rise in severe.)
   Eating abnormality.
   Sleeping problems.
   Elimination problems and enuresis.
2. Motor over- or under-activity.
   Whirling. Bodily dependence. Flexibilitas cerea.
   Dancing and darting.
   Co-ordination. Awkwardness. Choreoathetotic pattern hands after 6 months. Postural reflex persistence. Speech abnormalities, etc. Not used socially. Mutism. Physiological rhythms lose their normal patterns. Precocious puberty.

(*b*) Psychological tests.
  Bender test—vortical movement.
  Poor control. Conception of body image.
  Scatter and inconsistency.

(*c*) Psychiatric symptoms or reactions.
  All-pervasive anxiety. Echopraxia. Mannerisms.
  Mechanical voice. Extremes in response.

(*d*) Relation to key figures—peers, etc.
  Self-boundary loss.

Overintense reaction or withdrawal as response to others. Bender describes the three types of onset of the disorder. Below the age of 2 the condition is often difficult to differentiate from organic deficiencies although the motility disorder is typically unlike that seen in any neurological entity. A second group occurring about age 3½–4 which is more easily recognized. In the past many cases were termed Heller's disease. A third group occurring at age 10½–11 years.

The first attempt at description of the syndrome was made by De Sanctis in 1905 and Heller 1908. Bleuler had traced 4 per cent. of his hospitalized schizophrenics to childhood. Potter's criteria for the entity may be mentioned:

1. Disinterest in environment.
2. Dereistic thinking.
3. Disturbance of thought through blocking, symbolization, perseveration and incoherence.
4. Defect in emotional rapport.
5. Reduction of affect.
6. Alterations of behaviour. Increased motility and incessant activity or reduction of activity and stereotypy.

Bradley characterized schizophrenic symptoms in childhood as seclusiveness, daydreaming to excess, bizarre behaviour and inactivity.

Despert felt that the "presence of severe anxiety, inconsistent with reality was suggestive of schizophrenia". That "after the age of 3, the average child does not confuse thought and fantasy except under strong emotional stimulation".

Kanner (5) described the entity "autistic child" which later was included by other authors as a subgroup of the group of childhood schizophrenia. He collected 120 cases in this category having the following characteristic history:

"An almost universal report by parents that these children as infants had failed to assume the anticipatory posture before being picked up." There is addiction to "sameness"; passivity; quietness; withdrawal, a disregard of persons replaced by interest in the inanimate, and elaborate rituals which help to distinguish these cases from mental defectives.

Margaret Mahler (6) described a second group in the childhood schizophrenias, the "symbiotic" children, in which the child apparently developed normally to age 3, 4 or 5 when the schizophrenic process manifested itself.

"The disturbance shows itself when the maturation of the ego would normally effect separation from the mother."

Beata Rank (7) prefers to use the term "atypical" children for this group; her criteria for diagnosis:

"The most significant characteristic is that they are out of contact with reality and apparently without the need for communication with others."

Rank, Szurek and others describe similar pictures.

Kallman (8) in his genetic study diagnoses the illness on these criteria:

"Decrease of interest in the environment, blunted and distorted affect, peculiar conduct, diffuse anxiety and bizarre thinking."

Differential Diagnosis

Schizophrenia must be distinguished from mental retardation, aphasias, deafness, Heller's disease, organic disease of the brain and behaviour disorders.

Suggestive symptoms of schizophrenia are seclusiveness, unusual preoccupation with trifles, withdrawal of interest, mannerisms, changes in motility and excessive anxiety. (Bakwin) In differentiating from "organic brain disease", a history of trauma, early encephalitis; overactivity, restlessness and poor concentration with less marked anxiety; EEG findings, or signs of neurological disease are important.

Strauss (9) stresses in differentiating from "brain-damaged" children the seclusiveness, bizarreness, diminution of interest, sensitivity to comment in the schizophrenics, and the greater prevalence of foolhardiness over anxiety in the brain-damaged cases.

Bergman (10) considers factors important in differentiating the condition from mental deficiency: (1) Unusual developmental history. (2) Withdrawal from reality beyond expectation of mental age class. (3) Marked disturbance in interpersonal relationships. (4) Abnormal affect. (5) Incongruous psychological test results.

Differential diagnosis from neurosis as previously mentioned.

Psychological Examinations

Features of the response obtained in psychological test examinations will but briefly be mentioned in this paper. In distinguishing this condition from mental defect, one finds, according to Piotrowski, a higher score on verbal than performance scale which is often reversed in mental deficiency. The test results show scatter, unlike the uniformity in mental deficiency. The schizophrenic child may show a higher score on retesting. The figure-drawings in the schizophrenic group show a bizarre sense of body-image.

As to differentiation from organic brain syndrome, Sackler (11) writes:

"The evidence of organic factors on psychologic examination is different from that usually observed in psychoses with organic brain damage and post-encephalitic psychoses. Whereas, in the latter, there is generally inconsistency and an ability properly to carry out all those procedures indicative of organic damage, in the schizophrenic child this finding is variable. Thus one finds the schizophrenic succeeds in areas in which the classical groups would be helpless."

Prognosis and Treatment

In her follow-up study of cases between 1943 and 1951 which received metrazol (43), E.C.T. (100) and no specific treatment (50), Bender (19) found that 25 per cent. showed a later "fair" adjustment in treatment group, less in no-therapy group.

All cases, however, on clinical examination still showed a schizophrenic residue—motility, thought disturbance, defect in object relationships and dependence on the family (Kanner considers the prognosis poor in autistic children if language does not appear by 5 years). One-third of his cases improved; a similar figure to that of Bender.

Freeman and Watts (1950) (20) performed lobotomies on 11 cases of childhood schizophrenia before the age of 10 for destructive and assaultive behaviour. Limited improvement occurred after the operation and fantasies decreased considerably. Facial expression changed as revealed by the statement of a parent. "He looks at you instead of through you." Results were reported on a 6-year follow-up.

Escalona states that all cases in her study "relapsed after a temporary improvement on psychotherapy—either suppressive or expressive—at departure of therapist", although psychotherapy is the treatment of choice in many cases.

Aetiology

Although it might appear from the previous quotations of various workers in the field of child psychiatry that there exists some concordance of opinion on the description of the clinical entity, childhood schizophrenia, when one turns to the actual cases studied by these groups, and their findings, one is struck by the disagreement regarding aetiology.

As an example, Escalona describes her cases as "all free from organic pathology" (EEG, X-rays, etc.). Whereas Clardy finds an altered pneumoencephalograph and slow-waves on EEG in all his 9 cases in which Rorschach did not reveal "organicity". Two predominant groups appear to exist regarding aetiology; those who feel that early emotional traumata as exemplified by the "refrigerator parents" of Kanner or Spitz's work on anaclitic depression in institutionalized children, is all-important in the genesis of the disease and the group who feel that the emotional reactions of the environment are to a large extent secondary to a basic organic or hereditary defect in the psychotic child.

It will illuminate the issue to discuss these two groups in some detail as pertaining to the pilot study to be presented in this paper.

Primary Emotional Aetiologic Factor

Kanner, Rank, Despert, Geleerd, Bettelheim, Szurek, Mahler and others consider the emotional factors of greater importance in the aetiology of the condition. Psychodynamic factors such as maternal rejection/over protection, etc., during early oral period are to be considered.

Kanner originally stated (1943) that "we must assume that these children have come into the world with an innate inability to form the usual biologically protective affective contact with people, just as other children came into the world with innate physical and intellectual handicaps".

However, in later papers he discusses the importance of the early emotional factors in these children—the finding that the parents were characteristically "cold" unemotional intellectual people who raised their children "aseptically" and "by the book". He considers the genetic factor in these cases to be of small importance and "careful medical histories of pregnancy and delivery are negative insofar as any consistent pattern of pathological complications is concerned" (1956).

Starr (1954) (12) describes the development psychologically of the syndrome. Quoting him: "During the first 18 months the ego and functions, form and nature of object relationships and the flavour of the affective life are established."

The physiological symbiosis is disrupted by birth; the infant must develop a psychophysiologic symbiosis. It is a biological approximation to the intra-uterine symbiosis in so far as it achieves a good deal of physiologic regulation. But a new psychic dimension is added. At 18 months the infant undergoes a psychologic rebirth when another major disengagement from the mother takes place.

Unless the maternal buffer can successfully regulate or modify and increase or decrease appropriately the intrapsychic and environmental tension and stimuli impinging on the infant, adverse complications result. (Over-anxious mother may lead to symbiosis or inadequate unstimulating diluted relationship may lead to autism.)

The infant attempts to recreate the intra-uterine symbiosis but as it is not as constant (nutritional, thermal and postural), these attempts to restore intra-uterine physiological quiescence further the healthy ego development—an active reaching out into and contact with the environment. If the mother responds, this is transformed into a vitally needed external object."

The acquisition of locomotion and independence leads in the normal to commencing separation at the 18-month period. The symbiotic child "only feels safe in close proximity to the auxiliary ego; with the absence of the parasitic host, the child is thrown upon resources of its own inadequate ego and develops panic over separation."

Obsessive symptoms and perseverations are attempts to recreate the symbiosis—the "sameness" of a protected existence.

The differentiating feature from the simple dependent child is one of degree—the psychotic child cannot loosen the bonds due to ego-deficiency.

Starr believes the type of schizophrenia varies as to the time of deprivation. He does write that children vary in their object-seeking ability; they may have low "sending power" (Erikson) or "low voltage" (Gildea).

Primary Organic Aetiological Factor

As this paper is primarily concerned with factors of possible significance "organically" contributing to the ego-deficiency mentioned above, the workers in the field considering this factor as of importance will be discussed at greater length.

Anderson (1952) (13) states that she found it necessary to modify her view of the illness as determined by rejecting behaviour on the part of the mother to "a failure in the inter-personal relationship due to a very specific organic brain defect in the child". Where schizophrenic behaviour in an adult could be traced back into childhood in a continuous uninterrupted pattern, she was able to uncover strong evidence of an aetiologic factor of organic or anoxic nature having occurred early in their life.

She quoted as strong evidence of brain pathology, the visuo-motor co-ordination, confusion in figure and ground and lack of ability to integrate details into wholes.

"These children simply approach everything in a different manner."

They lack the ability to grasp, comprehend, and respond. Their associations are as confused as their perceptions. "It is not strange that their relationships with people are forever changing. In contrast, toys and books that stay put can be approached time and time again until the perception of them really registers."

"It also seems evident that strong feelings, positive or negative, associated with any stimulus, tend to be repeated whenever the stimulus is presented, even when the feeling generated is obviously unrealistic to the child."

This led Anderson to postulate that there is a perseveration of feelings as well as of motor sets.

In studying life histories, Bradley found consistent evidence that from early life these children were poorly equipped to deal successfully with the emotional stresses of "even the relatively protected life of little children".

Bergman and Escalona (14) describe the "thin protective barrier" which stimulates the erection of a substitutive precocious ego-development which may prevent normal function of more mature structures.

This thinness of the barrier is described as an innate inability to establish contact with people and a constitutional lack of protection against stimuli.

Peck *et al.* (15) in 1949 stated that in the majority of cases there was insufficient evidence of the child's having experienced gross mishandling. In their series of 200 cases, many of the parents had other children who functioned normally and they feel that this serves as a productive focus for comparison. A definite qualitative difference between schizophrenic and non-schizophrenic siblings emerged—in many cases this dated back to infancy.

A paper in 1952 by Rabinovitch (16) remarked that it was often difficult to differentiate between the primary reactions in the patient that serve as aetologic facts and secondary parental reactions to deviant behaviour.

He describes a consistent pattern in psychopaths but in regard to schizophrenia: "We have been impressed with the wide variety of early experience of the children. Some appear to have had intensive, consistent, warm mothering—others no meaningful mothering. No definite psychogenetic pattern has emerged.

Some workers have tended to correlate mechanical early mothering with later schizophrenia—our findings suggest generally a psychopathic rather than a schizophrenic outcome in these cases."

In 1954, Bender wrote: "Schilder stated that psychoanalysis neither in adults nor children had revealed enough psychogenic trauma to account for schizophrenia in contrast to simple neuroses."

Bender feels that the symptoms of neurosis often seen complicating the schizophrenic process are merely a reaction to the basic organic disease. In her 1947 paper she writes of the disproportionate number of dysrhythmic EEG records with periodic bursts of slow high voltage waves although agrees that these findings are inconclusive.

Clardy *et al.* (17) in 1941 found EEG abnormalities in all their cases which they dubbed "schizophrenic-like reactions in children". Furthermore the pneumoencephalograms revealed the presence of definite though minimal organic involvement. They quote Bradley and Jasper as having found in 82 cases of schizophrenia "no set pattern" but slow waves in 48 per cent. of the cases. In contrast, findings of Clardy suggested "cortical dysplasia". Kanner (5) found of 28 EEG reports, 21 showed normal pattern. Eickhoff (18) found no correlation between EEG and behaviour abnormalities.

Bender regards the illness as "always a pattern and not an isolated neurological sign of known brain pathways". She felt the postural reflexes found in many of the cases were nearly specific.

The higher incidence in males Bender and others feel supports the organic basis of the condition. (Bakwin found the death rates for all diseases of childhood higher in male infants.)

Genetic Factors

Disagreement exists among workers as to the importance of genetic factors.

Kallman (8) found the same difference in incidence of adolescent and childhood schizophrenia as in adults. A 17 per cent. incidence of the illness in partner of two-egg twin, compared with a 70 per cent. incidence in partner of one-egg twin.

Bender found of 143 children, 40 per cent. revealed one parent schizophrenic while in 15 per cent. this is the case in both parents. Some authors suggest that the "cold calculating" parents of Kanner's cases "sound schizophrenic". They feel the genetic element is strengthened by the fact that the same types of parent may have non-schizophrenic children.

Kanner is not impressed by the genetic factor. Of 200 parents, only 6 parents showed the illness, and of 400 grandparents, 12 revealed psychosis.

Bender, in comparing 30 schizophrenic children with a control group, found 12 fathers and 14 mothers schizophrenic in the former and 3 fathers and 1 mother in the latter.

She also considered the homes of the non-schizophrenic behaviour problem children more disturbed than the schizophrenic group.

Organic Brain Disease and Schizophrenia in Childhood (*Bender*, *Gesell*, *Yakovlev*)

Bender's view of the clinical criteria required for a diagnosis of childhood schizophrenia listed elsewhere in this paper reveal the "all-perversiveness" of the disorder.

In 1953 Bender discussed the concept of Gesell in regard to development of normal infants as contributive to the understanding of the pathogenesis of psychosis.

"All behaviour evolves from four basic physiologic functions:

1. Homeostatic mechanism.
2. State of consciousness.
3. Respiratory pattern.
4. Muscle tone.

"Tonic-neck reflex attitudes underlie all motor behaviour.

"Our study of infants shows that the schizophrenic infant retains all the features of the foetal infant as outlined by Gesell. No child can develop schizophrenia unless predisposed by heredity and precipitated by a physiologic crisis; the pattern of psychosis is determined by environmental factors."

Furthermore she points out that the unpatterned motor impulses seen in these children meet the compulsive, repetitive or perseverative tendencies which have been looked upon as hyperkinesis of brain damage. The condition is considered a developmental lag in the biological process.

In 1956 Bender wrote of the organic basis for the differentiation of the ego from the object.

"Tone defects and the tonic neck reflex domination of the organism's response to gravity and vestibular sensations is the crucial problem in distinguishing between self and non-self; ego and object. Gravity is the first sensory experience. The earliest relationship with the mother in which the child responds is in the setting and adjusting of body tone due to contact with the mother's body."

Bender points out that schizophrenic children under 2 years show the symptom of choreoathetotic pattern of the hands which is seen in normal infants in the first few months as the child discovers its hands and relates them to the visuo-motor pattern.

In his *Embryology of Behavior* and *Developmental Diagnosis* Gesell (21, 22), attempts to clarify the concept of personality and development of the mind with early patterns of muscle tone, growth, respiratory and sleep patterns.

Originally, in the foetus for example, respiration consists of a general response associated with neck muscle rhythms which slowly become individualized and separate from the "general response" of the foetus to stimuli.

He states, further, that the cerebral cortex does not undergo homogeneous development. Furthermore, respiration eventuates in part in vocalization; thereafter subvocal speech and thought. He states that the foetal infant also shows periods of catatonicity. He points out that man is functionally asymmetric—growth passes through a slow patterned development.

In describing this development, he writes: "Commencing with a primary nascent state, development becomes assimilative. When two or more traits combine, diverge or interweave; it becomes integrative when the trait acquires a second inseparable component; co-ordinative when a behaviour pattern of complexity emerges and synergic when it is incorporated into an action system." He states that traits *may reveal themselves originally as unrelated, cease, and eventually combine.**

Timing is of importance in this weaving pattern; if one mechanism is damaged, it may never be interwoven.

"It is easy to visualize how cerebral damage will interfere with developmental behaviour; how it will cause imperfect patterns; how some patterns may never be realized because one essential thread is destroyed."

Furthermore he points out that the tonic neck reflex, normal until 6 months, proves to be not a stereotyped reaction but a kind of matrix for growth of patterns of prehension.

"During much of his waking life the infant lies in this attitude which resembles a fencing stance. It promotes and channelizes vision to the extended hand and by gradual stages leads to hand inspection and to active approach and manipulation of an object."

The organism fatigues readily because of the vast amount of correlation which must be achieved between and within the visceral and sensorimotor mechanisms—shown by crying, drowsing irritability and fretfulness.

The 4-week old infant attends by means of "totalized reactions"—a full stomach absorbs his full attention; he is limited in his capacity of expressive moods and desires. Bodily activity is also reduced when reacting to social overtures.

Gesell summarizes: "All co-ordinations, both gross and fine, imply postural adjustments—adjustments of organism as a whole to its environing conditions. Locomotion is a dynamic, repetitive projection of posture; prehension and manipulation consist of a closely knit series of postural adjustments. The latter stage of synergic individuation, though, is independent of restricted postural sets."

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* This is illustrated by the symmetrotonic reflex as succeeding the tonic neck reflex at 16 weeks.

He states that attention is closely related to postural set and ocular fixation.

In describing the effect of organic cerebral damage in infants, Gesell points out that lesions of the nervous system in the infant tend to be diffuse as is the symptomatology. For example, infant hemiplegias are normally bilateral.

He considers that it is this diffuseness that accounts for the injury to the intellect and personality that so often accompanies neurological disease in infancy; that intelligence and personality are mediated by the whole cerebrum.

He concludes that "we believe that personality, like intelligence, has a structural basis, no matter how much that structure lacks compactness or precise configuration".

In 1949, Yakovlev *et al.* (23) described a few cases diagnosed as Heller's Syndrome "as a pattern of schizophrenic behaviour disturbance in early childhood". They referred to a description of the syndrome as showing rapid arrest of derived phases of behaviour (phases derived from experience living with others) with normal development of primordial and evolved phases. Many of these cases showed a history of birth trauma. Space as a dimension, Time as a duration and the experience of the body self in relating "I" to "not I" were not available.

Biopsy revealed a histological picture of a so-called "chronic cell change" of Nissl, a non-specific alteration which suggests a chronic state of anoxia.

He writes that Bender's contribution is important in stressing the failure of these children to establish a differentiated space relationship to their own body, that of other persons, etc.

"The differentiation of consciable experience of living to the level of the conscious experience of body/object/space relationship appears to be the cardinal prerequisite for the integration of derived into socially relevant behaviour."

Endocrine Abnormality and Question of Localization of Pathology

In the matter of aetiology it is difficult to distinguish primary causes and secondary results.

Sackler (1952) (11) lists the biochemical tests which seem significantly different in schizophrenia, e.g. insulin resistance, A.C.T.H. response, glutamic acid levels, adrenaline effect; histamine tolerance and blood-clotting phenomena.

As supporting evidence of possible importance of hormonal factors he states that the incidence of female schizophrenic children approaches that of males at adolescence. Many mothers of these children show thyroid dysfunction.

Evidence as to localizing brain lesions in the condition are conflictual. The small subgroup of schizophrenics—Heller's disease—do reveal (Weygandt) cortical changes, but on the whole research has failed to date to show a particular cerebral lesion associated with schizophrenia.

However, Kanner, who considers psychodynamic factors of extreme importance, states in his 1956 paper: "It must be recognized, however, that the neurological investigations of the integrity of central functions remain as yet in their clinical infancy and a negative result with current methods cannot be regarded as a conclusive demonstration of lack of pathology."

Kornfeld (24) considers that pathology may exist in an ultramicroscopic level; whereas Anderson and others believe there may be involvement of the last fibres to myelinate—the association pathways of the cortex.

Freeman and Watts found it necessary to sacrifice a great deal of frontal tissue to bring about any permanent improvement in their 11 cases; also usually resulting in considerable disability.

Gesell points out that the extent of neurological damage manifest in tests, etc. does not necessarily predict the degree of mental or intellectual deficit as is well known. Although a neurone destroyed cannot be regenerated it can sometimes be replaced by an unharmed compensating neuroblast. The damage may be protoplasmic in nature.

The infant of superior endowment may escape some of the permanent effects which an inferior child may suffer due to this wider margin of "neuroblastic resources and biochemical responsiveness".

"The most delicate damage may disfigure the molecular structure of cells and the integrity of lines of functional communication between the cells. Electrometric methods can locate a brain tumour but are insufficiently subtle to locate minimal injuries to brain substance."

Since methods of histologic, biochemical and electrical investigation are so inadequate, the method of retrospective history-taking may be tried in these cases to elucidate possible subtle differences between the sick children and their normal siblings. It appears that some workers have found a correlation, a few have not.

This type of investigation has been carried out on other disease entities—such disorders as mental deficiency, cerebral palsy, epilepsy, and, recently, behaviour disorders have constituted subjects for research. In the prospective setting, the work of Pennoyer, Caldwell, Ernhardt and Graham, etc. is (25) a further and probably more accurate method of investigation—a follow-up of a series of anoxic and control normal children and their subsequent all-round development.

B.—Prenatal, Paranatal and Postnatal Factors in Neurologic and Psychiatric Pathology

In the last few years considerable research has been carried out towards the investigation of the relationship between the following factors as affecting the developing foetus-infant and child and the subsequent pathology found in the nervous system.

1. Abnormalities in prenatal and paranatal periods.
2. Relationships to maternal age, birth-order and previous reproductive loss.

All the studies to be mentioned are concerned with these factors; however, Lilienfeld (1956) (26) states in the summary of his paper on the relationship between maternal and foetal factors and mental deficiency: "In an analysis we have not been able to take into consideration such postnatal conditions as lead poisoning, head injury and encephalitis which may be causal factors in mental deficiency. Their relative importance is not certain, but there is no doubt that they do result in mental deficiency. Further studies to take these into account should be carried out."

Pasamanick, *Lilienfeld* et al. *A Retrospective Study*

A paper in May, 1955, summarized the findings of this group (27a and b) series of cases from a given area and given birth period were compared with normal controls selected by matching the next birth certificate in the same period by the place of birth, maternal age and race.

Prenatal and Paranatal Factors

Complications of pregnancy considered were: Toxaemias, bleeding during pregnancy, diseases associated with but not related to pregnancy (heart disease, diabetes); breech presentations; dystocia and abnormal pelvis; pyelitis, hydramnios, premature separation of the placenta praevia, prolapse of the cord, malpresentations other than breech.

Neonatal Factors

Convulsions, cyanosis and asphyxia.

Other Criteria

1. Total number of pregnancies.
2. Number of abortions and premature births.
3. Number of neonatal deaths.
4. Length of labour. Operative procedure (low, mid, high forceps, version).
5. Birth weight.

The number of cases studied and results of these studies shown in Table I.

TABLE I

Type Disorder	No. of Cases	Years of Birth	Source of Cases
Cerebral palsy ..	561	1940–1947	New York crippled children's register
Epilepsy	564		Baltimore Hospital
Mental deficiency	1,081	1935–1952	Clinics, hospitals, schools
Speech disorder ..	424		
Behaviour problems	1,151	1940–1945	Referred by public schools

Findings were as tabulated in Table II.

TABLE II

Cerebral Palsy

	Cases	Controls
Complications pregnancy: .. .. .. (predominantly non-mechanical)	38%	21%
Prematurity	22%	5%
History of stillbirths	35% more in months of cases	

Average age of mother with first child greater in case group.

The authors show that these data support Little's hypothesis that palsy is due to trauma, as many abnormalities of pregnancy are associated with the same condition.

They find here that "it seems the various complications which show a greater degree of association with infant loss are also more likely to be associated with cerebral palsy".

Mental deficiency and epilepsy show a similar correlation. In the former, there is a relationship with the maternal age and birth order, whereas in epilepsy a history of a greater number of abortions.

Speech disorder showed no correlation.

Behaviour Disorders (28)

Again here an increased frequency of non-mechanical complications of pregnancy was found with prematurity. Moreover, no association was found with maternal age or previous reproductive casualty. These cases were divided into two groups; one showed little correlation whereas the confused, disorganized, hyperactive group were associated mainly with the above factors.

The cases were those referred by schools as undisciplined, manifesting behaviour sufficiently deviant to be deemed beyond the scope of the school personnel to correct (three-quarters of cases were referred for nonconformity).

A rather mixed group fell symptomatically into this class and probably included many neurotics and possibly some psychotic children. However, diagnoses are not offered. Symptoms included apart from the typically aggressive as reported by teachers:

1. Daydreaming, lives in world of his own. Plays alone. Stares into space.
2. Fear of people and things, nightmares.
3. Disorganized children who can't concentrate; are negativistic, make strange noises. Hyperactive.

Series studied, 471 cases and 359 controls. (Next child of same sex born in same city in same classroom.)

All cases tested I.Q. over 80.

Results appear less marked than other studies.

The authors conclude in this paper: "Of all the factors studied, a relationship is present only with certain complications of pregnancy and prematurity. Other factors—maternal age, birth order, abnormal neonatal conditions and a maternal history of abortion are not associated with behaviour disorders. Since there is an inter-relationship between all these factors, it would appear puzzling that some of these factors are not associated. On the other hand, consideration must be given to the fact that in dealing with behaviour disorders we are concerned with a group of conditions of heterogeneous aetiology. This would tend to diminish the strength of any true association.

"In addition, the type of neural damage resulting in behaviour disorders is obviously minimal relative to the gross type of damage that would manifest itself in cerebral palsy. A greater association is found with the classical 'brain-damaged' group."

Previous Studies in the Effect of Anoxia and Birth-Trauma in Neuro-psychiatric Disorders

They refer to numerous previous studies on the effect of anoxia on animals (Windle, 29) where it appeared possible to produce behavioural malfunction analogous to human deficiency in learning ability, quoting Darke's (30) findings of such a relationship in humans. Interestingly, the last author used siblings as controls as is the case in the present paper. He found that a statistically significant difference in mental status existed between a group of asphyxiated children and the control group of siblings.

Bridge, studying epilepsy, found in 742 cases, 41 per cent. showed a history of brain injury, 29 per cent. both heredity and injury, 14 per cent. heredity. Fender in a group of 37 epileptics found 25 had histories of complications in pregnancy; whereas of a control group of 40 children with rheumatic fever, only 4 showed abnormal birth histories.

They furthermore discuss the well-known close correlation between foetal death and complications of pregnancy.

Schreiber (32) in 1938 found in his series of 500 patients with cerebral symptoms (convulsions, mental retardation, spasticity) 70 per cent. showed a history of apnoea.

Preston (31) in 1945 reported on 132 cases of anoxia and their subsequent behaviour at age 10 years. Seventy-four per cent. of the total showed hyperactivity; 33 per cent. apathy, and 28 per cent. epilepsy. Postnatal infection aggravated these symptoms. Of these children 49 per cent. were rejected by parents, 64 per cent. "showed no liking for anyone", 68 per cent. were disliked by others. The parents complained that they "do not take in what is said". Social contact with other children appeared difficult to endure. A few of these cases certainly appear to be classifiable under the heading of childhood psychosis.

Preston concludes that in the presence of any suspicion of anoxia in prenatal or postnatal periods the babies cannot be considered normal until a sufficient period has elapsed for damage to neurones undeveloped and unmyelinized at time of anoxia to be disclosed, revealing no interference in the unfolding of maturational mechanisms.

Gruenwald cites the importance of rubella occurring during the first or second month of pregnancy as resulting in 100 per cent. maldevelopment in the foetus; the importance of irradiation during pregnancy and the Rh factor in the development of mental deficiency.

Cole (33) found the single most important factor in the aetiology of neonatal asphyxia is prematurity; other factors include the manner of labour, sedatives and anaesthesia.

Penrose (34) in *Biology of Mental Defect* may be quoted as revealing a method of approach toward the subject of the inter-relationship between genetics and trauma and their relative importance, although he appears to overstress the former.

"Instead of attempting to ascribe our causes either to nature or nurture we can simplify the objective and merely ask which of the two events was the earlier."

(*a*) Genetical: remote or recent.

(*b*) Environmental, prenatal, para- or neonatal disease.

He does state that postnatal injury must be considered as important in psychiatric defect. Encephalitis studies have shown irregular lesions of the basal ganglia are common whereas defects of the pyramidal tract are less likely to follow the infection in childhood.

In contrast to these studies, Norval (35) found no relationship between anoxia and convulsions in the survivors.

Penrose found only 11 defectives out of 1,200 whose physical condition and histories warranted the certainty of birth injury. Campbell (1950) (37) found no association between asphyxia neonatorum and defect in 195 cases and controls.

Lilienfeld writes of these studies:

"One major difficulty is that they have attempted to isolate one feature of the pregnancy experience and study its relationship to defect, as exemplified in the study by Keith and Norval where no correlation between prolonged labour and defect was found."

Greenhill in *Obstetrics* (1955) (36) reports a study by Perlstein and Barnett on the aetiological factors in cerebral palsy.

Prenatal

1. Heredity.
2. Infections in first 3 months of pregnancy.

(Pyrexia in mother during labour requires 7 per cent. more O_2 for every degree and sulfanilamide therapy may replace one-third of the oxygen.)

3. Prenatal anoxia: maternal anaemia. Cord difficulties.
4. Trauma during pregnancy.
5. Rh factor responsible for 3 per cent. palsy cases.
6. Maternal diabetes, X-rays.

Paranatal Factors (accounted for 60 per cent. cases)

Anoxia; obstructions; malpresentations; cerebral haemorrhage (not more than 3 per cent. due to forceps, holding back of head and induction of labour).

Sudden labour.

Bleeding tendency.

Postnatal. Accounted for 10 per cent. cases. This study is mentioned as it also tends to throw some light on the relative importance, percentage-wise, of these factors.

In summarizing their various studies Pasamanick, Lilienfeld, Rogers *et al.* postulate a "continuum of reproductive casualty".

"We are no longer justified in thinking of the conditions studied as representing distinct, separable and individual clinical entities but must rather think in terms of cerebral injury which is manifested by Cerebral Palsy, Mental Deficiency, Epilepsy and/or behaviour disorder depending on the degree and area of injury."

They found the same factor in those conditions as also influencing infant loss as comprising lethal and sublethal components.

Gruenwald's comment regarding the importance of timing as of greater moment than specific traumata is apt here. He states that widely differing factors, genetic and extrinsic, may have a similar effect by acting upon the embryo at a stage when a definite pattern of sensitivity of various parts exists.

Prospective Study—Importance of Anoxia

A recent prospective study done by Graham, Caldwell, Hartmann *et al.* (1957) (25) on anoxia as a significant perinatal experience came to the following conclusions:

1. Cord blood oxygen saturation appears to reflect very transitory levels of oxygenation. Since it is not necessarily closely related to even the immediate neonatal condition, it would not be surprising if there were no relationship with more remote events.

2. It seems necessary, consequently, to employ a less exact but more meaningful clinical criterion of anoxia. Second, even though a clinical criterion

is used, it should permit some ordering as to degree in addition to satisfying the usual scientific demands for objectivity and reliability.

3. There is considerable variability in the postnatal rate of recovery of anoxic infants. Measurement of these differences provides a way of identifying those infants who may be most likely to show residual effects.

4. "Events believed to lead to foetal anoxia were associated, in our subjects, with relatively greater impairment in performance on newborn behaviour tests than either postnatal anoxia or non-mechanical delivery complications."

Defects in Retrospective Studies

Lilienfeld, Pasamanick *et al.* enumerate some difficulties in such retrospective studies, especially in the field of birth records. Neonatal convulsions, cyanosis, asphyxia and maternal factors are under-reported on the hospital records except for the more severe forms.

The present study compares the factors prenatal, paranatal and postnatal occurring in the schizophrenic children and their normal siblings. As this study does not concentrate on genetic factors, evaluation would appear to be difficult. It is practically impossible, though, in such studies to eliminate all the variables. It may be said that, although members of a family do not have the same heredity, they are genetically considerably more alike than persons chosen at random from the general population.

Graham *et al.* discuss the differences in prospective and retrospective studies.

"To ask how frequently paranatal complications may be associated with a certain defect and to ask how frequently a certain defect is associated with paranatal complications is not the same thing. Even if all mentally retarded children had been anoxic at birth, there would still remain many non-retarded anoxic children, as mentally retarded children would constitute only 40 per cent. of an anoxic group when one baby out of every 20 is anoxic."

Furthermore the importance of adequate control groups is stressed. Results may either be invalidated or obscured because differences between groups are insignificant compared with variability within groups. Darke's method of pairing cases with siblings affords one solution, which is also used in this study.

The Plan of the Present Study

The present study is attempted in order to reveal subtle differences in the case and control (sibling) groups as far as birth traumata and childhood illnesses below the age of two are concerned. An effort is made to shed some light on the question: Why does one child show process schizophrenia while the siblings may be normal or merely neurotic?

This study does not attempt to prove or disprove the importance of an organic or psychogenic aetiology in the illness. Both obviously contribute but the qualitative difference between childhood psychosis and neurosis is too marked to be explained by psychodynamic factors alone.

In a study mentioned previously, Lilienfeld found some difference, though not of statistical significance, between cases classed as behaviour disorder and controls as far as trauma was concerned, in the "clear-cut" "brain-damaged-driven" children as a subgroup.

Authors differ as to their reports on the incidence of birth injury and other traumata in the histories of these children. It appears, however, that there has been little attempt at recording these data *per se*. By the method of sibling-control we can possibly arrive at the subtle differences in the two groups.

It may be objected that mothers would naturally tend to over-report physiological trauma, etc. as a defence against their own emotional responsibility in these cases—however, in meeting this objection, it may be mentioned that the culture of today tends to lend itself to emphasis on psychodynamics which should reflect in the mother's attitude. Secondly, in an attempt to meet this objection, the author studied the charts of non-psychotic, non-brain-damaged children attending a child guidance clinic, noting the frequency in which a history of birth trauma, etc. was given for the maladjusted (neurotic) child in comparison with the adjusted siblings. As will be seen in the chart, the incidence was practically nil in marked contrast to the schizophrenic cases (Table III).

TABLE III

Mothers' Estimate of Organic Trauma in a Series of Neurotic Children
(*Birth-Histories, Illnesses before 2*)

1.	S.	Worsening pattern with two later "well-adjusted" siblings.
2.	F.	No difference.
3.	B.	No difference.
4.	A.	No difference.
5.	K.	No difference.
6.	W.	At 2½ years, hyperpyrexia.
7.	W.	Pregnancy normal but after age 6 months patient a "walking pneumonia".
8.	B.	No difference.

The limited number of cases arose from fairly strict criteria of selection; the fact that many of the parents had moved since the year of consultation at the clinics and that many happened to be only children.

Plan of Study

Number of cases: 15 (present ages, 4–14).
Number of controls: 33 (siblings), ages, 2–25.

Sources: From Washington University Child Guidance Clinic, County Child Guidance Clinic, Cripple Children's Association, private practitioners, and Child Evaluation Clinic in St. Louis, Mo.

As diagnosed at the Child Guidance Clinic Conference attended by psychiatrists, social workers, and psychologists. Records, 1952–1958.

Criteria for Diagnosis of Schizophrenics in this Study

1. Onset before age 11 years. Motor awkwardness and inco-ordination. Under- or overactivity.

2. A history of a period of normal "milestone" development prior to onset of illness.

3. Bizarreness of behaviour, mannerisms, etc.

4. Speech abnormalities present, e.g. mutism.

5. Psychological test results reported as schizophrenic.

6. All-pervasive anxiety.

7. Disinterest in environment, seclusiveness, unusual occupation with trifles, interests in the inanimate, especially with mechanical gadgets.

8. History of sleep disturbance.
9. Reported by mothers and peers as "different" from other children.

The diagnoses of the Child Guidance Clinic Conference were rechecked when the mother was interviewed.

All cases showed the majority of symptoms listed above; the overall picture of the child being of supreme importance.

No case showed definite evidence of clinical neurological disease, although a considerable number did not receive a complete neurological examination. Only a few EEG and pneumoencephalogram reports were available in these cases.

The mothers were interviewed and birth and hospital records obtained where possible. The mothers were asked to describe the symptomatology of the patient; the adjustment of the siblings and to answer certain questions on pregnancy, birth-history and diseases of childhood (Table IV). Control siblings did not reveal symptomatology as listed classifiable under case criteria.

Cases revealing evidence of classical "brain damage" were rejected.

It is interesting to note that the parents of these children did not appear to fall into a single personality category.

TABLE IV

Questionnaire

(*After Table compiled by Child Evaluation Clinic of St. Louis*)

1. HISTORY

A. Identifying information Date................
Name.................................. Age........ Sex........ Race........
Present during examination..

B. Family History:
(*a*) Father: Living.......... Age.......... Age at birth of patient............
Serious illnesses..
(*b*) Mother: Living.......... Age.......... Age at birth of patient............
Serious illnesses..
(*c*) Consanguinity...................... Details..............................
(*d*) Children. List all pregnancies in order and indicate outcome:
1............................... 6...............................
2............................... 7...............................
3............................... 8...............................
4............................... 9...............................
5............................... 10...............................
Totals: Pregnancies............ Live births............ Abortions............
Stillbirths............ Living............
(*e*) Diseases in lineals and collaterals: M.R............... C.P..............
Convulsions.............. Allergy.............. Sensory or motor handicap (specify).............. Diabetes.............. Mental illness..............
Tuberculosis.............. Cancer.............. Heart disease..............
Kidney disease.............. Other..
Elaborate on any positives in above listing ....

C.
History of Pregnancies:
(*a*) Contagious: Rubella............ (When)............ Mumps............
Influenza............ Lues............ Others............
(*b*) Medical: Heart disease.................. Hyperthyroidism..................
Hypothyroidism..................
(*c*) Obstetric: Uterine bleeding.............. Threatened abortion..............
Toxaemia............ Ankle oedema............ Albuminuria............
Hypertension............
(*d*) Nutrition: Quality of diet......../......../........ Total weight gain........
good fair poor
(*e*) General condition (physical and emotional) during pregnancy. Describe and estimate whether good, fair or poor ....

TABLE IV—*continued*

(*f*) Time when medical care began..............................
Quality of prenatal care......../......../........
good fair poor
(*g*) Others: RH incompatibility............ Trauma............
Irradiation .... Others ....
(*h*) Notes ....
....

D. Personal History:

(*a*) Birth: Of EA. Sibling:
1. Maturity: Full term.......... Premature.......... Birthweight..........
2. Medication: Anaesthesia.................. Sedation..................
3. Presentation: Cephalic.................... Breech....................
Transverse.................... Other....................
4. Labour: describe..
....
5. Delivery: Spontaneous.......... Forceps.......... Caesarean..........
Version..........
6. Cord ....
7. Neonatal: Normal........ Respiration delayed........ Weak cry ....
Blue baby........ Resuscitation........ O2........ Incubation........
Trauma........ Jaundice........ No. of days........ Convulsions........
8. Notes..
....

(*b*) Development of Children:
1. Motor: Age held head up................ rolled over................
sat alone............ stood alone............ walked alone............
2. Language: Age talked words................ sentences................
3. Social: Age smiled.................. Age toilet trained..................
(*c*) Feeding problems: Vomiting........ Regurgitation........ Colic........
Difficulty in swallowing................ Constipation................
(*d*) Immunization complications ....
(*e*) Diseases (state age at which occurred):
1. Contagious: Measles.......... Chickenpox.......... Mumps..........
Pertussis..........
2. Meningitis............ Encephalitis............ Pneumonia............
3. Traumatic: Head injury............ With loss of consciousness............
With convulsions............
4. Surgical ....
5. Others..

E. Present Complaint:

(*a*) Details of handicaps (include age first noted). (Recheck of Clinic history and symptomatology patient and siblings.)
....
....
....

KEY TO TABULATION OF DATA

In the tables (V) following, representing the findings on individual case records, criteria used in tabulating the data obtained from mothers' reports (Table IV in this paper) and hospital records include (cases):

1. Age of child at time interview with mother.

2. Age of mother at birth of child.

3. Birth order. No twins in this study.

4. Prenatal factors include any infection or condition of mother both associated with and unassociated with the pregnancy which is generally considered of significance by workers in the field as resulting in possible trauma to the foetus.

5. Paranatal: Actual labour and neonatal condition of the infant. Birth weight.

6. Postnatal includes all traumata after birth to age 2 years; e.g. infections, toxins, etc.

Only those diseases are tabulated which occurred prior to the onset of the psychosis.

The sole listings under heading "case" are factors which are not common to the siblings; listed under siblings are factors peculiar to the controls.

A developmental history was taken to detect retardation of either case or control. One of the siblings of the 34 diagnosed by the Child Evaluation Clinic as mentally retarded (Case No. 9) was not included as a control in the final percentage tabulations. This family does, however, include normal siblings.

Below the case record is tabulated the sibling chart. The value of compiling data on the 2-year-old controls may be questioned. In all of these families, however, the 2-year-old was not the sole control. In retrospect the mothers reported a qualitative difference between the psychotic child as an infant and their youngest sibling.

The head "siblings" also includes birth weights and a listing of abortions and their timing in relationship to the live pregnancies.

Marked deficiencies occur in the *hospital records* owing to differences in recording detail in the various Institutions. Length of labour was rarely recorded; a few records revealed merely the birth weight. In many cases the records were unobtainable as children were born outside of the St. Louis area, etc.

"Symptomatology of patient" and "hospital records" complete the table on the individual cases.

Factors utilized in compiling the percentages in the Summary are marked by asterisk.

A difficulty arose in classifying the severity of the specific traumata—medical induction of labour was, for example, not recorded as significant because of lack of clarity of indications. An obstetrician examined the factors used in compiling the percentage charts (marked by asterisk) and concurred regarding their relative importance.

TABLE V

Individual Case Loadings Tabulated from Questionnaires, Interviews, and Hospital Records

Case 1. K.S. (Female):

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
11	39	2	*Child Rh positive. False labour 7 months.	Shortest labour 7½. *See hospital record.	

Siblings (2):
28 Rh^{-ve} (Female) 7½.
9 Rh^{-ve} (Male) 7½.

Common Factors:
Heredity. Retroverted uterus. Mother Rh^{-ve}.

Symptomatology:
Onset at age 4. Poor school achievement though scattered. Asocial. Sleep disorder. Bizarre behaviour. Temperature abnormalities.

"Never runs a temperature even if severely ill."
EEG shows some abnormality.
Pneumoencephalogram normal. Psychological shows no evidence of retardation.
At present in special school. Tested by numerous neurologists who found no evidence of "brain-damage" syndrome.

TABLE V—*continued*

Hospital Record:

Patient: False pains 1 month prior delivery. Admitted.
Midforceps. Cord around neck. Nine hour labour*.
28 year old: 22 hour labour.
9 year old: 12 hour labour.

Case 2. C.C. (Male):

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
14	29	3		Prolonged birth. Foot presentation.*	Up to 3 months, undernourished.*

Siblings:

25. (Male), 7.
23. (Male), 7. Rickets*.
7. (Male), 6. 12.
3. (Male).

Common Factors:

"Several relatives" retarded.

Symptomatology:

Unsatisfactory scholastic achievement, although scattered. "Different from all other children." Asocial. Excessive fears of mechanical gadgets. Terrified of rag dolls. Awkward. Prefers inanimate to persons. Passive.

Treated at Child Guidance Clinic.

Hospital Record (obtainable on patient and last two children):

Patient: Only birth weight recorded.
7 year old: } Normal deliveries. (Full record.)
3 year old: }

Case 3. C.B. (Male):

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
8	22	2		6 pound. Smallest.	Drank oil at age 2, (onset schizophrenia) Severe pneumonia. Hospitalized week. "Unconscious."*

Siblings:

9. (Male), 7½.
3. (Female), 7½.

Common Factors:

Cousin of father retarded.

Symptomatology:

Hyperactivity at 2 years. Requires tranquillizer. Fears are all-encompassing. Poor coordination. Unpredictable behaviour. Asocial. Treated at Child Guidance Clinic.

Hospital Records:

Patient birth record: Normal.
10 year old: Normal.
Record of patient at age 2: Admitted 2 hospitals. Five day admission present. Aspiration pneumonia. Ingestion kerosene and choking as result.

Case 4. J.D.G. (Male):

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
6	32	1	At 4½ and 7 months "premature" labour for 1 week (toxaemia). Uterine bleeding. Mother received severe burn at 6 months necessitating hospitalization.*	Shortest labour.	Head injury with baseball.

Siblings:
5 (Male), less bleeding than with patient.*
2½ (Female), induced due to "weak contractions".

Common Factors:
Brother of husband in psychiatric hospital. Hypothyroidism of mother in first 2 pregnancies.

Symptomatology:
Treated at Child Guidance Clinic. Mutism. Parents opposed to clinic. Recommendation *re* institutionalization. Global fears. Sleep disorder. Asocial. Hallucinations and destructive behaviour at times. Not "cuddly" as a baby.
No birth record.

Case 5. R.S. (Male):

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
5	31	2	Anaemic entire pregnancy. B 12 continually tried.*	Hospitalized 2 weeks prior delivery. P.V. bleeding. Premature rupture of membrane Longest labour.*	

Siblings:
11 +(abortion at 2 months).
10 (Male), 6.
1 (Female), staining in first few months.*

Common Factors: Nil.

Symptomatology:
Bizarre behaviour. Interest in the inanimate. Typical psychological. Motor inco-ordination. No bowel training. Asocial. Marked sleep disturbance. Fearfulness global. On tranquillizer. Onset first months. Strabismus. Operation at 3½ years. Wore glasses at few months.

Hospital Record:
Patient: 16 hour labour. Bleeding. Previous hospitalizations.
10 year old: Normal.
1 year old: Normal.

Case 6. S.B. (Female):

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
9	30	3		6·8. Patient "one week early". Tried to hold her back. Ether last minute—other siblings full anaesthesia. Short labour. "All medical personnel out of town."*	Dropped by brother as a baby.

Siblings:
15 (Male), breech* (see hospital record).
13 (Female), 6·3. Measles with hyperpyrexia.*
8 (Male), 7·0.

Common Factors:
Mother felt poorly during all pregnancies.

Symptomatology:
Private referral. Slow to react. Awkward. Bizarre mannerisms, sounds, withdrawal. Reading problem. Passive and aggressive outbursts. Psychological showed psychotic core.

Hospital Record:
Nausea during first 4 months all pregnancies.
15 year old: Pregnancy delivered at term. No note of position. 2,820 gm.
13 year old: Normal. Scanzon. Maneouver (foroccipito—posterior).
9 year old: 2,950 gm. 3 hour labour.
8 year old: 3,100 gm. 9 hour labour.

Table V—*continued*

Case 7. L.C. (Male):

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
14	21	All pregnancies thereafter abortions	At 3 months severe fall down steps by mother. Later on 2 occasions. Bed-rest for long periods required.*	4·6 pounds. Premature. Short labour. Incubation.*	Whooping cough and pneumonia at 2 months. Practically died. Mastoid operation.*

Siblings:

1. 17 (Female), 11.
2. +Male child died at 18 months of pneumonia (No. A3 patient).
4. 1954, died at 7 months.
5. Aborted at few weeks
6. Aborted at 4 months } Hospitalized.
7. Aborted at 5 months

Diagnosis—habitual abortion.

Common Factors:
Father maladjusted. Deserted wife. Paternal aunt psychotic.

Symptomatology:
Patient now in State Hospital. Quite different from sibling as baby. Kept household upset. Bizarre behaviour. Awkward. In many institutions. Also chorea at age 11 for 6 months. EEG and pneumonencephalograms detect nil abnormal.

A case where much psychological disruption at time pregnancy of patient.

Hospital Record:
17 year old: Not available.
14 year old: "Apparently full term but seemingly premature infant."

Case 8. D.K. (Male):

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
10½	23	1	Mother depressed.		Pneumonia at 8 months. Hyperpyrexia.*

Siblings:
8 (Female), 6·15.
5 (Male), 7.
3 (Male), 4·14, Placenta praevia.* Caesarean. Infant normal.*

Common Factors:
Paternal aunt in State Hospital. All highstrung. Father psychotic.

Symptomatology:
Blatant schizophrenia. On tranquillizer. For State Hospital. Asocial. Problem to siblings. Sleep abnormality. Giggling. Poor co-ordination. Destructive. Tantrums. Different as infant. Perseveration. Echolalia. Echopraxia. Smelling objects. Psychological factor: unhappy marriage.

Hospital Record:
10½ year old: No record available.
8 year old: Normal.
3 year old: Premature birth. Normal child. Caesarean section. 4.14.

Case 9. B.D. (Female), Negro:

Mother a poor witness. Hospital record more revealing.

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
6½	28	3	Nil	Nil	Nil

*See Hospital Record.

Siblings:

11½ (Female).
Abortion 2 months.
10 (Male).
8 (Female).
5½ (Female). See under Symptomatology.
4 (Male).
3 (Female).

Common Factors:

Antiluetic therapy, 1944 (Hospital record).

Symptomatology:

"Different from others." Sleep problems. Hallucinations. Poor co-ordination. Destructive behaviour. Asocial. Spells of anger and anxiety. Speech disorder. Sudden running spells. Treatment at Child Guidance Clinics.

5½ *year old:* Retarded. Cleft palate.

Hospital Record:

11½ year old: (Male), 7.6. Normal.
9 year old: (Female), 6.16. Normal.
6½ year old: (Female), Breech. Condition apparently favourable.*
5 year old: (Female), (defective) acute enterocolitis. Diarrhoea acidosis.
4 year old: (Male). Normal.
2 year old: (Female), 8.10. Normal.
One abortion listed as having occurred in 1935.
1944: Antiluetic therapy.

Case 10. J.G. (Male):

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
13	27	1		7.8. Traumatic birth marks. Paediatrician told parents patient would always need extreme care because of difficult birth experience.*	Mother run down during puerperium. X-ray thymus infant.

Siblings:

Abortion at 3 months. One year prior to birth patient. 10 (Male), 6.8.

Common Factors:

Hypothyroidism during pregnancies. Nephew of husband psychotic.

Symptomatology:

Passive. Asocial. Poor co-ordination. Global fears. Echolabia and perseveration. Sameness. Originally diagnosed as retarded. Psychologicals clear.

Hospital Records:

13 year old: Mother hospitalized for 3 weeks. Delivery per high forceps over episiotomy 3,450 gm. ROA. Previous miscarriage noted.
10 year old: 7 day hospitalization, 3,100 gm. Manual rotation from ROT to ROA. Low forceps. Infants normal.

Case 11. D.S. (Male):

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
7	28	2		8. Induced labour.	19 months. Severe hyperpyrexia. Tonsillitis. "Dying."*

Siblings:

10. (Male), 8.

Common Factors:

Retroversion uterus.

Symptomatology:

Mutism. Seen in Child Guidance Clinic for 2 years with slight improvement. Sleep disorder. Co-ordination poor. On phenobarbital. Global fears. Definite psychological diagnosis. EEG: Slow record at 5 years. Marked over- or under-reaction to illness.

Hospital Records:

10 year old: 3,520 gm. Normal. Prenatal record normal.
7 year old: 3,470 gm. Medical indication of labour with artificial rupture of membranes.

TABLE V—*continued*

Case 12. B.R. (Negro female):

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
12	24	2	Excess weight gain over 50 pounds month. Pneumonia 4 months.*	8.8. Labour long and traumatic. "Did not see baby after birth due to vaginal abscess". Isolated 10 days.	Severe diarrhoea as baby.*

Siblings:

Abortion 3 months prior patient.
9. (Female), 8.6.

Common Factors:

Hyperemesis during both pregnancies. Paternal brother psychotic.

Symptomatology:

Mutism after age 2½. Treated at Child Guidance Clinic. Asocial. Global fears. Bizarre behaviour.

Hospital Record:

12 year old: Normal delivery. 8½. Abscess vagina. Baby isolated 10 days.
10 year old: 3,690 gm.

Case 13. J.G. (Female Negro):

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
4	30	3		6.16	At 10 months hospitalized for rash. Alopecia: hyperpyrexia. Four weeks hospitalization during onset of psychosis.*

Siblings:

6. (Male), 5.4½.
5. (Female), 6.12.

Common Factors:

Nutritional deficiency all but first. Antiluetic therapy mother. Pre-eclampsia all 3 deliveries.

Symptomatology:

Scattered retardation as of age 10 months. Chews on shoes, etc. Asocial. Awkward. Strays off. Mutism. Destructive. Mechanical interests.

Hospital Record:

History antiluetic therapy.
6 year old: Pre-eclampsia. Normal delivery.
4 year old: Pre-eclampsia. Normal delivery.

Case 14. B.L. (Male):

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
15	25	1		8.13. Excessive haemorrhage. Forceps scars. Difficult puerperium.*	

Siblings:

12. (Female), 7½.
8. (Female), 7.10.

Common Factors:

Mother's sister psychotic.

Symptomatology:

Enuresis. Asocial. Passive. Recommended to institution. Decompensating schizoid.

Birth Records: Not available.

Case 15. B.B. (Male):
Mother poor witness.

Age	Maternal Age	Birth Order	Prenatal	Paranatal	Postnatal
1	2	3	4	5	6
13	24	1		Patient's delivery more difficult. (Considered not significant as patient oldest).	

Siblings:
11. (Male).
8. (Female).
6. (Male).

Common Factors: Nil.

Symptomatology:
Passive child. Numerous therapies. Asocial. Scattered performance at school. Co-ordination poor. Bizarre mannerisms. Interest in inanimate. "Seem to get relief from a spanking".
Visceral difficulties: School problems. Psychologicals clear.

Birth Records:
Patient born outside of State.

SUMMARY OF FINDINGS

1. The importance of heredity in these families is somewhat difficult to assess in a study of this nature. In an approximate estimation 3 per cent. of the parents, their siblings, and grandparents' families showed evidence of psychosis whereas the incidence in the general population is about ·85 per cent. There were no cases of consanguinity in this study.

2. Forty per cent. of the 15 cases showed a history of traumatic prenatal factors, in contrast to 9 per cent. of the 33 controls. No case or control received irradiation during prenatal phase in this study. Significant to ·05 per cent (40).

3. The importance of paranatal factors is revealed in the difference of occurrence in cases and controls (53 per cent. compared to 6 per cent.). Significance ·01 per cent.

These findings are in contrast to those of Lilienfeld *et al.* in that paranatal factors appear prominent here. In this study, however, it was impossible to separate the mechanical procedures used, from the early indication for their use (complications of pregnancy) as was done in their study, due to the deficiency in the hospital records.

It may be noted that one premature infant in both case and control groups is recorded.

4. The marked differences in incidence of postnatal illness before age 2 is striking (46 per cent. in cases; 18 per cent. in controls). Significance: ·01 per cent. Whether these severe illnesses are a direct cause of the psychosis, though, is unclear as classical encephalitis usually presents a somewhat different neurological picture.

No cases of obvious asphyxia livida or pallida were found in hospital records. On mother's subjective account, two children "remained in incubator". No head injury reported by the mother resulted in loss of consciousness although most head injuries were found in the case group. Head injuries were therefore not included in the tabulation.

5. Twenty per cent. of cases were preceded or followed by abortion; only 3 per cent. in controls. Not considered significant.

6. The mean age of the mother at the birth of the group of cases and controls shows no significant difference.

7. Sixty-six per cent. of the cases were males, 33 per cent. females, whereas 57 per cent. of controls males, 42 per cent. females.

8. Recording data from birth records alone (most were markedly defective on the pregnancies of the mother—though they may have appeared in the records of private obstetricians) and neonatal condition of the child showed 10 per cent. with prenatal, 60 per cent. paranatal trauma cases compared to 5 per cent. prenatal and 10 per cent. paranatal in controls.

9. The general rate of abortions in these two groups—about 14 per cent. —is not greater than that found in the general population.

10. Table VI indicates that only 2 cases of the 15 revealed little or no difference in the "traumatic loading" between case and siblings in the family.

TABLE VI

Number of Cases Revealing No Loading Case or Loading of Control (Sibling)

1. Case No. 8 (hyperpyrexia at 8 months) shows loading of 3 year old sibling. (Placenta praevia.)
2. Case No. 15 reveals no positive factors regarding heredity or any evidence of birth or postnatal organic trauma in either case or controls.
   Two of the 15 cases revealed blatant serious emotional problems during pregnancies with the patients.

SUMMARY

The present study appears to reveal a somewhat larger incidence of prenatal trauma among the cases than among the controls; a vast and significant difference in paranatal factors, and significant differences in postnatal trauma before age 2.

A larger number of cases than controls were preceded or followed by abortion.

Little difference occurs in sex of patients and controls, showing a slight predominance of males in the case-group. The mean age of mothers at birth in case and control groups are similar.

The increased incidence of these factors does not necessarily indicate brain damage, although these facts point in that direction.

It may be held, however, that emotional factors in the mother (during pregnancy) may so alter maternal biochemistry, etc., as to result in a larger number of traumata to the foetus. However, only in two cases do we find gross maternal psychic trauma during pregnancy, though a study of this type does not uncover subtle psychodynamics.

Similarly, the increased incidence of postnatal vulnerability to infection, etc., may be a secondary phenomenon in an "emotionally deprived child". It appears, though, that neurotic and psychopathic children may have as disturbed an emotional background as these psychotic children. Even Spitz's findings have been subject to criticism by Pinneau (39).

It is concluded therefore that organic factors may play an important part in laying the ground for the illness childhood schizophrenia, although this ego-deficiency may never appear if emotional atmosphere is supportive. That the pathology involved is at present speculative is clear, as may be noted in the quotations of other authors mentioned in this paper.

Kanner's statement that the "medical histories of pregnancy and delivery are negative in so far as a consistent pattern of pathological complications is concerned" in his autistic subgroup does not necessarily negate the present study, which attempts to reveal subtle differences in the histories of cases and siblings, that may not be apparent if the case history is considered on its own. Of 11 of Kanner's original cases in 1942 (38), 8 revealed slight organic insults pre- or postnatally; one experiencing convulsions.

He writes (1956) of his autistic cases: "There are a group of parents who do not fit the described psychological pattern, and we find frigid parents who do not give rise to autistic children."

Moreover, the present study includes other subgroups of childhood schizophrenia.

ACKNOWLEDGMENTS

The author gratefully acknowledges the helpful counsel of Dr. P. Painter, also of Drs. A. Kaplan, M. Cox, S. Rosenzweig, L. Cass, Miss M. Cannon and others of the Washington University and St. Louis County Child Guidance Clinics, where this work was carried out, for the use of case records, as well as Dr. B. Caldwell of the Child Evaluation Clinic for the use of their questionnaire and Mr. P. Ley of Netherne Hospital, Surrey, for statistical evaluation.

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HALLUCINATIONS AS A DISORDER OF GESTALT FUNCTION

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THE authors wish to describe and discuss a patient suffering from a sub-acute organic psychiatric syndrome, who appeared to have visual hallucinations. One of us (F.F.) had been interested in the attempt of K. Conrad (1953a, b) to apply Gestalt Theory to the psychiatric syndromes due to coarse brain disease. When he heard of this case, he felt that the psychological approach of Conrad would explain the patient's unusual symptoms. The case was under the immediate care of Dr. A. Forrest and psychological testing had been carried out by Mr. E. Macpherson. The three authors decided that the case merited publication in view of its considerable clinical and theoretical interest.

The patient, D.B., a 69-year old gardener, had enjoyed good health until January, 1957. One night, while reading the newspaper, he found that the letters were turning upside down, and although he could see the print, it made no sense to him. He was seen by an ophthalmologist and his eyesight was reported to be satisfactory. Coming home from work one evening in April, 1957 he found that he was unable to grip the handlebars of his bicycle with his left hand. He staggered while walking, his speech became slurred and he complained of pain in the back of the head. He spent ten days in bed and during this period his speech became normal and his grip improved. He began working during the second week of June, 1957 but after a few days he again lost the power in his left hand and became confused. He was admitted to Roodlands Hospital and was transferred to the Eastern General Hospital, Edinburgh, on 6 July, 1957 under the care of Dr. J. A. Bruce. Examination at that time revealed weakness of palatal movement on the left side, weakness of the left hand, nominal aphasia and apraxia affecting both hands. He was euphoric but also irritable. Lumbar puncture on 8 July, 1957 revealed a clear fluid under a pressure of 180 mm. The protein content was 152 mg. per cent., cells were within normal limits, the colloidal gold curve was 2333444311 and the Wassermann reaction was negative. Repeat lumbar puncture on 15 July, 1957 revealed clear fluid with a protein content of 300 mg. per cent. A diagnosis of degenerative cerebral vascular disease was made, the patient made steady improvement and was discharged home on 31 July, 1957.

On 10 August, 1957 the patient had an epileptic fit, on 13 August, 1957 he had another fit and on 18 August, 1957 he had two further fits. Later during this day he was re-admitted to the Eastern General Hospital and a week later had a further fit while in hospital. This was a classical grand mal seizure. He then passed into coma, was pyrexial and incontinent for twenty-four hours. On 27 August, 1957 he was seen by one of us (A. Forrest) at the request of Dr. J. A. Bruce. As he was confused, restless and difficult to manage in a general hospital ward his admission to the West House division of the Royal Edinburgh Hospital was arranged.

On admission (2 September, 1957) he showed no abnormality on examination of the nervous system. Impaired percussion note and diminished air entry was noted over the right lung base. Mental examination revealed that he was pleasant in manner and co-operative during interview. He sat quietly, spoke clearly and at a normal speed. He had marked difficulty in naming objects and used paraphasic expressions. For example an ash-tray was described as "a thing for cigarettes". He perseverated at times. He understood and carried out both written and spoken commands. He was able to repeat words but made many mistakes in writing to dictation. He was emotionally labile but his general mood was one of euphoria. His orientation for place was correct but not for time. Memory for recent events was poor. He tended to interpret events in the ward in military terms. Thus on one occasion he said he was going to be put on a charge for striking another patient and usually referred to patients walking in the grounds as "the squad". He was unable to do simple calculations but could repeat four digits forwards and four digits backwards. Probably the most outstanding feature was his paraphasia. Thus he referred to one of us (Dr. Forrest) as Notts Forest (a football team) and to another colleague (Dr. S. G. Laverty) as "the Italian sounding in upper London". It should be noted that Dr. Laverty has a Southern English accent.

The patient was referred to Mr. E. Macpherson who reported "When first tested on 11 September, 1957 the patient was cheerful and co-operative but exhibited short bursts of irritability. The Wechsler Bellevue Scale (Form I) showed a Full Scale I.Q. of 95 with Verbal and Performance I.Q.s of 103 and 78 respectively. The patterning of sub-test scores reflected a rather marked degree of intellectual impairment. His raw scores in Digit Span were F-6, B-3. In the Arithmetic sub-test he succeeded in only the first five items. He experienced considerable difficulty in all Performance Tests except picture completion. He failed to obtain any credits in either the second or third items of Object Assembly. In the third item (the hand) he remarked at the end of three minutes 'I think it is a cemetery but I can't put it together'. This might suggest some degree of failure in the organization of perceptual experience, of a type frequently encountered in organic states. The Bender Gestalt raw score was 129. The forms which he reproduced were recognizable but showed the sort of gross distortion seen in coarse brain disease."

The euphoria and paraphasia continued for about three months but meanwhile a new feature emerged towards the end of September, 1957. The patient claimed that he could see messages written on the outside wall of the hospital and on the wall of the ward corridor. From his own ward he could see across to the Female Wing and saw the words "Hearts Football Club" on the wall and nearby, where several small windows lie close together, the words "Free Church". He saw his own surname written on the door of the ward kitchen and on the adjacent corridor wall. He could be persuaded that these were misinterpretations but was not really convinced. Later (in the middle of November, 1957) he no longer saw the words but remained more or less convinced that he had seen them in the past. His paraphasic speech disturbance slowly improved and by the beginning of December, 1957 he was very well and had complete insight into his illusions, which he now called "hallucinations".

Meanwhile extensive laboratory investigations had been carried out in an attempt to elucidate the aetiology of his illness. In brief, haematological examination revealed no abnormality, blood urea nitrogen was normal, the blood Wassermann reaction was negative and liver function tests gave normal results. X-rays of skull and chest revealed nothing apart from a slight elevation of the right diaphragm and reduced translucency at the right lung base. This condition was thought to be inflammatory and was treated with antibiotics. Two further specimens of cerebro-spinal fluid were examined and found to contain persistently high protein values, the last figure (28 October, 1957) being 144 mg. per cent. An EEG revealed an excess of slow activity (4–5 c./sec.) from post-central, temporal and frontal regions. Some low voltage delta (3 c./sec.) was recorded from both temporal regions. On the basis of these investigations a diagnosis of cortical thrombo-phlebitis was made.

Psychological tests were repeated on 29 October, 1957. The psychologist reported as follows:

"When the Bender Gestalt was re-administered the form distortions were again seen but a new feature also emerged. Whereas previously he had made a good attempt at Card 2* he now reproduced the columns as one continuous line, using instead of the circles, the letters GOD. These letters were repeated twelve times and extended from one side of the page to the other. It seemed, therefore, from this second examination that not only was perceptual organization disturbed but that a restructuring of the perceptual field had occurred, resulting in a misinterpretation of visual experience."

Detailed clinical examination was carried out on 12 November, 1957. The paraphasic disturbance was found to be quite marked but variable. He was able to name five out of seven common objects, but when shown a calendar he said "An almanac—you shift the dates for yourself". In conversation he often used military terms instead of the appropriate word, thus he referred to the ward as the camp. He was orientated for time but could not give the name of the hospital, though he knew it was a "nerve hospital". His memory for events in the acute phase of his illness was very poor but he could give a good account of events in the two weeks prior to testing. He was able to recall accurately an address and telephone number after three minutes. He understood written and spoken commands and carried them out correctly. He was able to write to dictation and copy a written sentence. However he had difficulty in reading from a typed sheet as the words moved about and lost their meanings.

He was discharged on 24 December, 1957 and was followed up as an out-patient. When last seen on 16 February, 1959 he was very well and had no complaints about his health. He was working part-time as a gardener and admitted to no subjective difficulty in speech or memory. Detailed clinical testing revealed no abnormality apart from a patchy amnesia covering the acute phase of his illness (July–October, 1957). The Bender Gestalt test was administered at this time. The psychologist reported "The Bender Gestalt now gives results which are within normal limits (raw score 25)".

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* Thirteen columns, each consisting of three circles, placed at an angle from the vertical.

Although the authors can find no similar case in the literature, Bartlet (1955) has described a patient, who had attacks of dysphasia, visual perseveration and metamorphopsia due to a left-sided parietal or temporo-parietal lesion. This author regarded the visual perseveration as a confabulation, the content of which was determined by the Law of Prägnanz. He suggested that in his patient, at least, difficulties in figure ground differentiation were dependent on the left temporo-parietal region. Thus although Bartlet's patient did hallucinate, he did so in attacks in which other visual and dysphasic phenomena occurred. This is quite unlike the case described here.

The psychological disorders which occur in psychiatric illnesses due to acute, subacute and chronic brain disease have not been discussed very much in English literature except in so far as they may be due to focal lesions. In the German literature there has been considerable discussion of the psychopathology of the amnestic syndrome. As this syndrome is the expression of subacute damage to the brain it is likely that any psychological theories applicable to it might be applicable to psychiatric conditions due to subacute brain damage which are not typical amnestic syndromes.

Although the memory disorder is quite prominent in the amnestic syndrome, other psychological disorders occur so that from time to time it has been suggested that the memory disorder is one aspect of a more general disorder. Pick (1915) pointed out that the amnestic patient rigidly holds on to ideas which contradict one another, so that once a train of thought is produced it continues despite contrary information from without until some powerful internal or external stimulus forces it into another track. Grünthal (1923 and 1924) agreed with Pick's findings but claimed that there was also an inadequate formation of relationships between current percepts, presentations and thoughts on the one hand and total experience on the other. He regarded this as a disorder of set (*Einstellung*). Thus the patient is unable or has difficulty in getting away from a given train of thought and is unable to form relationships with ideas which lie outside this train of thought. This leads to new material being registered only with difficulty and even if it is registered recall is difficult. Thus for Grünthal the classic disorder of impressibility may be partly due to the more general disorder of comprehension.

Bürger Prinz and Kaila (1930) extended the idea of a disorder of set and also pointed out that the patient with an amnestic syndrome is easily satisfied in his attempts to find a meaning or, as Bürger Prinz puts it, there is a defective need to find meaning (*Sinnfindungsbedürfnis*). Thus these patients are unable to make adequate constructions out of details which are presented to them either spatially or in a temporal sequence.

Van der Horst (1932) has claimed that in the amnestic syndrome the temporal signs of the individual memories are lost, so that the patient is unable to recall the memories because of their lack of chronological arrangement.

In all these theories one can see one common idea, namely the fragmentation of experience and the lack of temporal or spatial organization of experience. Grünthal, Bürger Prinz and Kaila have both stressed the disorder of comprehension, and the latter authors the formation of false constructions due to the defective need to find meaning. The illusions in our patient could be understood as a disorder of comprehension of details and the formation of a false construction. However, we feel that this interesting symptom can be better understood on the basis of the theory of disordered "Gestalt Function" of Conrad (1953a, b). This author considers that there is a "Gestalt Function" which is the most general basic property of psychic life. There are two psychological operations of this "Gestalt Function" which are closely connected. There is the operation of integration by which a new content of experience is integrated with the total trace field and then there is the operation of differentiation by which an integrated part of the total trace field is brought into prominence when required. In brain disease the ability to form new effective gestalten, the ability to extract individual contents from the total field and to encompass the total field at any one time may all be disordered to some degree.

In the operation of impression or registration the new material must be organized into the total trace field. It must also, where necessary, form a paired gestalt with the material which precedes or follows it. When there is a disorder of "Gestalt Function" then this integration into the total trace field and the formation of paired gestalten is also disordered and presents as a disorder of impression. In this case the new memory lingers on for 40–50 seconds when it fades or if a new impression follows within 50 seconds the first memory is extinguished by retroactive inhibition. Conrad has called this type of memory defect "Minute Memory".

The disorder of Gestalt Function affects other psychological activities such as perception, comprehension, intellectual productions, reproduction of remote memories and so on. In the operation of comprehension the patient may only be able to grasp details and is unable to comprehend whole gestalten. He is liable to enumerate details, fasten on a detail then falsely interpret the detail thus forming a new false gestalt. The disorders of comprehension can be seen as disorders of different sets of figure ground relationships. There is a series of grounds which in their turn become figures against the ground of a higher order. Thus there is Ground 1 which is the ground against which the figure stands out, when an individual is observing a test picture. Then there is the total visual field which as Ground 2 forms the background for the test picture as a whole. Then the total visual field forms the figure against Ground 3 which is the total current psychic functioning of the individual. This total current functioning is experienced against the background of Ground 4, which is the temporal sequence of the whole of the subject's life. Finally there is Ground 5 which is the objective system of relations in which all knowledge is experienced. Thus for example, the knowledge that the picture is a part of a psychological test introduced by a given psychologist for a certain reason.

In coarse brain disease the figure ground relationships may be disordered in all five of these grounds. Thus in Ground 1 the disturbances are usually slight and the disturbances become more severe with the increase in complexity of the ground.

In Ground 1 many details may be successfully enumerated although the total gestalt is usually not recognized. Details may be incorrectly comprehended. In Ground 2 the disturbance is greater and a false orientation may be built up out of critical details. Thus one of Conrad's patients made up a false orientation of a restaurant on the basis of a sign post in the hospital grounds and a terraced garden. The extraction of the figure from the ground is even more difficult in Ground 3 and shows itself in the total spatial disorientation and a similar disturbance in Ground 4 shows itself in a temporal disorientation. The construction of a correct system of relations in Ground 5 is rarely possible. Thus the most severe disorder is in the extraction of a given content from the total field present at any given time and the construction of the correct system of relations in connection with it.

It is natural to pass on from the disorder of comprehension to the disorder of intellectual production which is usually present in subacute organic states.

Conrad asked one of his patients to give him the names of all the trees he knew. He produced several names, repeated the same names but he did not know why he was doing so. Thus he was unable to remember the nature of his task but continued to do it. In more difficult tasks such as telling the story of Adam and Eve he failed completely.

This disorder of intellectual production might help to explain the peculiar speech disorder which occurred in our patient and is well known in organic psychoses, especially in Korsakoff states (Clarke, Wyke and Zangwill, 1958). This consists of misnaming, paraphasia, discursiveness and, in some cases, bizarre forms of expression. Owing to the disorder of Gestalt Function the extraction of the appropriate thought content is difficult so that the verbal expression is likely to be approximate. A pre-verbal image may well be treated in the same way as a detail in a picture and only an approximate name attributed to it. Apart from this the consciousness of the task may disappear as in Conrad's patient. This would lead to a fairly correct beginning to the task but as the patient proceeded with it the progress of thought would be determined by a very vague consciousness of the task and there would be a tendency to derailment but the vague consciousness of the task would prevent a complete deviation, thus giving rise to paraphasia. However, this in itself does not explain the paraphasic thought disorder as Conrad's patient did not show it well. There obviously must also be a marked inner drive (*Antrieb*) which keeps the train of thought going.

The Block Design Rotation Effect can also be fitted in with Conrad's ideas. Shapiro has shown that the designs made with Kohs Blocks are often reproduced in a rotated position and the degree of rotation is greater in brain-damaged than in normal subjects (Shapiro, 1951, 1952, 1953; Shapiro and Tizard, 1958). However, if normal subjects work with a cue reducing mask and on a table covered with black felt then the rotation effect is much greater. Thus it seems that the brain-damaged patient cannot take advantage of cues such as the table edge, the graining of the table surface and so on. In other words the patient cannot encompass the total gestalt but deals with the card and its reproduction as if they were isolated details. Rotation would be expected to take place in accordance with Gestalt laws of perception so that one would expect a figure to be produced with the best symmetry and pregnance. This is in fact what happens. Thus the misinterpretation of detail and the rotation of block design can both be understood as a failure to relate figure to ground and the formation of a new partial gestalt in accordance with Gestalt laws of perception.

On the basis of this theoretical background we believe it is possible to understand our patient's interesting symptom. He misinterpreted details occurring in his visual field. The irregular marks on the outside wall and scratches on inside walls and doors were seen as words. A new Gestalt was formed out of a few details. The patient's disorder of the appreciation of form was clearly shown in the Bender Gestalt test. His difficulty in reading typewritten words also confirms his Gestalt Function disorder. It will be remembered that words seemed to move about, or in other words details of his perceptions did not maintain a reasonably firm relationship to one another. One can understand that they might therefore have formed false relationships to one another. Once the new Gestalt had formed, the difficulties of encompassing the whole field at any one time would make it difficult for the patient to correct this false simple Gestalt and he would naturally be reluctant to relinquish the tiny piece of order which he had extracted from the chaos around him. The presence of these illusions for several weeks is probably also related to the patient's inner drive. He was euphoric and somewhat restless during the time he had the illusions and looking back he admits to being puzzled about his surroundings. It could thus be argued that this patient had a marked inner drive (*Antrieb*) which could lead to a greater positive misinterpretation of the environment than many other patients with subacute brain disease.

The content of the illusions can be understood as arising from the patient's preoccupations. He was a keen football enthusiast and was interested in the results of all Football League matches. This probably accounts for his paraphasic misnaming of Dr. Forrest as Notts Forest. The subject of football was probably frequently brought to his mind by the daily visits of Dr. Forrest. It is, therefore, not surprising that when he was in a situation which permitted the formation of an illusion, he saw the words "Hearts Football Club" which referred to the well-known local football team, the Heart of Midlothian Football Club. When last seen the patient said that when he was in hospital, he was frequently puzzled about his surroundings and could not understand why he was detained. The idea of becoming free was probably uppermost in his mind. This would partly account for the illusion "Free Church". In the society to which he belongs the word "free" is frequently associated with the word "church". It is possible that in this case the grey stone walls of the hospital reinforced this association. As the patient was frequently asked his name it is reasonable to assume that his name and identity were often in his thoughts. This would explain the repeated illusions when he saw his name written on walls and doors.

His mistake on the Bender Gestalt test when he wrote "God" for "o" is very interesting. The phrase "Oh God" is frequent in prayers and is also often uttered in hopeless desperation. The patient appears to have partly retained some idea of the task he had been set, namely that he had to write down a series of letters, but owing to a paraphasic derailment he wrote the word "god" instead of the letter "o". It will be remembered that he wrote the word "god" repetitively across the page although the series of "o"s were in columns at an angle to the vertical. The isolation of the part from the whole may have led him to write the word "god" across the page instead of at an angle to the vertical.

SUMMARY

A subacute organic state, probably due to cortical thrombo-phlebitis, is reported. The patient saw various words written on walls and doors and referred to this phenomenon as hallucinations. This symptom is explained as an illusion based on a disorder of Gestalt Function. Conrad's theory of disorder of Gestalt Function in organic psychoses is discussed.

ACKNOWLEDGMENTS

We wish to thank Dr. T. A. Munro, Physician Superintendent, Royal Edinburgh Hospital, for permission to publish this case, and Dr. J. A. Bruce for access to his case notes.

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THE COMPARATIVE PSYCHOPHARMACOLOGY OF SOME MESCALINE ANALOGUES

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INTRODUCTION

THERE are, in the main, two principal methods of biological research into the problem of causation of schizophrenia. In the first, or direct method, studies are made of the body fluids and of the metabolism of schizophrenics in the hope of turning up some toxic factor or error of metabolism. Such studies are currently under way in a number of centres and, although many claims as to positive findings have been made, none of these has as yet been substantiated and the majority have actually been refuted by subsequent analysis. These studies have been directed by two main hypotheses of the causation of the illness described in a previous communication (14). Now it is clear that one great difficulty entailed in using this approach is that our basic knowledge of neurochemistry and neuropharmacology is still extremely limited. The very complexity of the neurochemical processes of the brain would seem to offer a large number of possible loci of metabolic disturbance, any of which might be responsible for the onset of schizophrenia. Thus, we can say that the *probable* results of all such investigations at present will be purely negative, i.e. we will discover that the given metabolism of injected adrenaline, serotonin, etc., is normal in the illness. Thus, the second, or indirect, method becomes increasingly important. This consists of two parts. The first is implied merely by the general statement that the advance of neurochemistry and neuropharmacology may disclose other areas of function in which specific hypotheses of the causation of the illness may be constructed. The second consists of a detailed study of the precise mode of action of known psychotomimetic agents. Knowledge of the mode of action of mescaline and LSD-25 in detail would pinpoint areas for research in the metabolism of schizophrenics. Unfortunately, however, very little seems to be known at present of the mode of action of these drugs. Most of the work that has been done has been carried out on LSD-25 (see e.g. the annotated bibliography put out by Sandoz Inc., Hanover, New Jersey, 1958). However, the important field of the structure-activity relationships (SAR) of mescaline seems to have been strangely neglected. The research programme here would include the synthesis of a number of analogues of mescaline according to systematic principles to determine the role the details of its molecular structure play in the mode of action. These analogues would be subjected to a number of tests—psychopharmacological, neurophysiological and neurochemical—*comparison between the results of which* would give important information not only of the SAR of mescaline but also of the details of its mode of action and the interrelationships between behavioural, neurophysiological and neurochemical factors involved that would help us explain the former effects in terms of the latter, which reduction is the main aim of biological science. The present paper reviews the little that is known at present about the SAR of mescaline and then reports some new studies in the psychopharmacology of this field.

REVIEW OF PREVIOUS LITERATURE

De Jong (4) and Noteboom (10) reported that several analogues of mescaline, including dimethoxyphenylethylamine (II, Fig. 1), produced "catatonia" in various animals. However very large doses were used as well as only qualitative means of evaluation of behaviour and a large variety of drugs tested produced this result. However IV (Fig. 1) was inactive in large dosage. Epstein *et al.* (6) found that p- and m- methoxyphenylethylamine and methylenedioxyphenylethylamine (III, Fig. 1) stimulated sympathetic terminations in cats but not rodents and were also CNS stimulants. 3,4-dimethoxyphenylethylamine (II, Fig. 1) was a pure CNS depressant. Grace (7) confirmed these results and showed that 3,5-dimethoxy-4-ethoxy- and 3,4-diethoxy-5-methoxyphenylethylamines were also CNS depressants. Elphick and Gunn (5) found that substitution of a hydrogen atom on the β-carbon atom by a methoxy group in mono-, di- and tri-methoxy phenylethylamines weakened physiological activity quantitatively but not qualitatively. The mono- compounds were still CNS stimulants and the other two were purely depressants without sympatheticomimetic properties. Reti (12) stated ". . . the slightest structural changes destroy the typical effects of mescaline. Until now no natural or synthetic compound with the pharmacological properties of mescaline has been found." He stated however that Lewin had attributed certain hallucinogenic power to anhalonidine. He also reported that trichocereine (N-dimethyl mescaline) produced excitation in rats but that 550 mg. ingested by Ludueña produced no apparent effects. Benington *et al.* (2) synthesized a number of mescaline analogues and tested them qualitatively on cat behaviour. In a dose of 25 mg./kg.

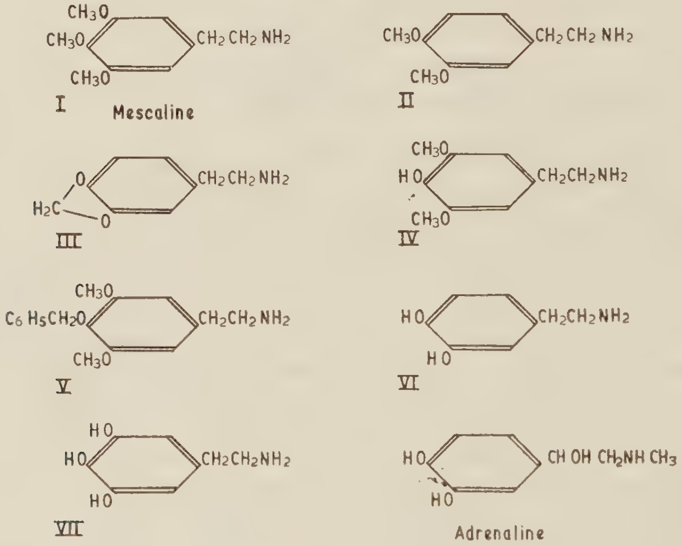

FIG. 1.—The formulae of some mescaline analogues; named in text.

they found that a number of these produced strong rage reactions as evidenced by growling, hissing, aggressive behaviour, withdrawal, pilomotor activity, salivation and pupillary dilation. The compounds were 3-methyl-, 4-methyl-, 4-chloro-, and 3,5-dimethyl-4-methoxy-phenylethylamines. Among the compounds that did not produce this reaction were 3,4,5-triethoxy- and 3,5-dimethoxy-phenylethylamines. Ethyl, isopropyl and t-butyl groups in the 4-position of phenylethylamine produced progressively less rage response in cats. Clark *et al.* (3) showed that 2,4,6-triethoxy- and 3,4-dimethoxy-phenylethylamines were strong inhibitors of succinic acid dehydrogenase; 4-hydroxy-3,5-dimethoxy-phenylethylamine (IV, Fig. 1) and N-methyl mescaline were moderate inhibitors and mescaline itself had no action on this enzyme. Alles (1) has reported that 3,4-methylenedioxy-phenylethylamine (III, Fig. 1) has no hallucinogenic properties but that the corresponding isopropylamine derivative (126 mg.) has. Peretz *et al.* (11) showed that 3,4,5-trimethoxyphenylisopropylamine (TMA) is somewhat more strongly hallucinogenic than mescaline. Gunn *et al.* (8) stated on a basis of their experiments that, in the case of amphetamine-like compounds, an isopropylamine derivative is more stimulating to the CNS than the ethylamine compound and the methylenedioxy compound is similarly more active than the dimethoxy derivative.

MATERIAL AND METHODS

The drugs were tested using the Winter and Flataker rat rope-climbing test (15). Male white rats (weight around 100 grammes) of the Sprague-Dawley strain were collected five to a cage and trained to climb a 5-foot rope under hunger drive. The time taken to climb the rope was recorded. In each experiment four control runs were taken (the first being discarded), the drug was injected into the peritoneal cavity and then each rat was run at regular intervals (given in Table I) for 60–80 minutes. A cut-off time of 60 seconds was used. The results were then expressed as (mean time in seconds for the drug runs per cage) minus (mean time in seconds for the control runs per cage) for each dose level for each drug (Fig. 2). Alternatively the time course of the drug effect was plotted, again as mean climbing time under drug action minus control time (Fig. 3). Three experimental designs were used. In experiment 1, a Latin square design was used of 3 cages for 3 drugs all at the same dose level. In experiment 2,

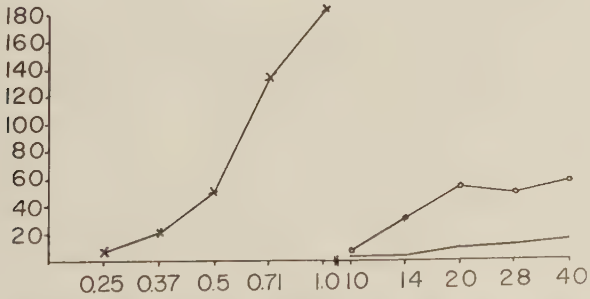

FIG. 2.—Dose response curves; abscissa, dose of drug in mg./kg.; ordinate, mean increase in climbing time per cage (in seconds) for all runs after injection produced by drug. Crosses = 1-adrenaline; circles = 5-hydroxy-dopamine; dots = dopamine.

3 such series were run with three dose levels. In experiment 3, 15 such series were run in a complex Latin square design to give each of 3 cages of rats each of five doses of 3 drugs in order to be able to prepare dose-response curves.

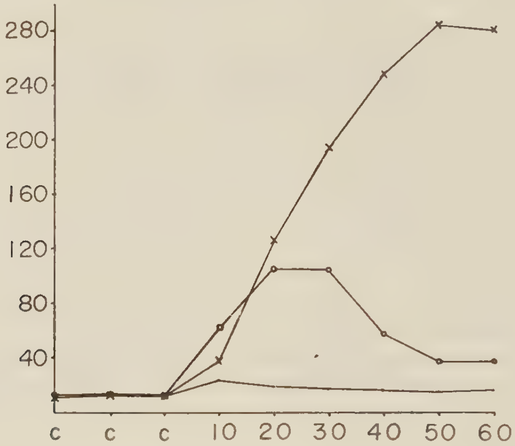

FIG. 3.—Time course of drug action at highest dose given. Abscissa, three controls and then time after injection in minutes; ordinate, mean climbing time for each time period in seconds. Code as in Figure 2.

RESULTS

Experiment 1. Here the effects of mescaline were compared with the effects of 3,5-dimethoxy-4-hydroxy-phenylethylamine (IV, Fig. 1) and 3,5-dimethoxy-4-benzyloxy-phenylethylamine (V, Fig. 1). The results are given in Table I

TABLE I

Each Figure gives the Mean Increase in Climbing Time per Cage in Seconds Over the Mean of the Three Initial Pre-injection Control Runs. The Effect of Saline Control Runs is also shown. Each Point is the Mean of 15 Readings

Drug	Dose mg./kg.	Minutes after Injection					
Experiment I		10	20	30	40	50	60
Mescalin	50	39	130	172	238	235	178
IV	50	4	1	2	3	8	3
V	50	192	248	233	246	230	219
Experiment II		5	20	35	50	80	
(*a*) Mescalin ..	50	120	173	176	186	160	
II	50	90	85	38	20	3	
Saline	—	15	2	15	8	7	
(*b*) Mescalin ..	25	84	144	134	123	65	
II	100	203	232	228	192	85	
Saline	—	8	15	8	12	8	
(*c*) Mescalin ..	30	70	103	120	136	96	
II	60	87	115	107	97	60	
Saline	—	18	3	8	15	18	

and show that V is substantially more active than mescaline whereas IV is without activity.

Experiment 2. Here the effects of mescaline and 3,4-dimethoxyphenylethylamine (II, Fig. 1) were compared using saline controls. The results given in Table I show that II has about one-half the activity of mescaline. Unfortunately no mono-methoxy derivatives were available to test in this series.

Experiment 3. The effects of dopamine (VI, Fig. 1) and 5-hydroxy-dopamine (VII, Fig. 1) were compared with those of l-adrenaline. The results are shown in the dose-response curves of Figure 2. Figure 3 shows the time course of action of the highest dose of each drug. The marked behavioural effects of l-adrenaline stand in interesting contrast to the almost complete lack of activity of dopamine given by this route. Substance VII shows a moderate degree of activity. The slow time course of activity of the adrenaline may reflect local vasoconstriction hindering adsorption. As all these three agents are pressor agents it was thought that some of these effects might be due to the development of hypertension. Rats were therefore anaesthetized with nembutal (35–50 mg./kg. i.p. or i.m.) and one carotid artery was cannulated and connected to a mercury manometer. Control blood-pressure readings were taken and then the drugs were injected i.p. at the highest dosage used. Di- and trihydroxy phenylethylamine caused a small, inconstant and delayed rise of B.P. of some 10–15 mm. Hg. L-adrenaline (1 mg./kg.) caused a rise of 20–30 mm. Hg. A dose of 0·5 mg./kg. caused a rise of 10–15 mm. Hg. L-adrenaline (5 gamma) given intravenously to these same rats caused a brisk rise of 40–50 mm. Hg. It was thought, therefore, that these elevations of blood pressure might not be the sole cause of the behavioural response. It is well known that adrenaline is relatively inactive given parenterally and it is thought that it is quickly inactivated in the liver to which organ drugs given intraperitoneally would largely be directed by entering the portal system. Therefore some metabolites of adrenaline might be partially responsible for the behavioural effects. In this regard l-metanephrine and l-vanillyl-mandelic acid, both in a dosage of 2 mg./kg., were tested in rats by the technique here described. Both, however, were quite inactive. In some cases our adrenaline solutions underwent, on standing at room temperature for some time, spontaneous oxidation to "pink adrenaline". An amount of this solution that had contained 1 mg./kg. of adrenaline was similarly tested and was also found to be quite inactive. The marked effects produced by this dose of adrenaline had been totally lost by the mixture of reddish-orange oxidation products that make up "pink adrenaline". The mechanism of production of the behavioural effects of adrenaline given by the intra-peritoneal route therefore remains obscure. This effect may be allied to the interesting states of adrenaline stupor induced by similar doses of adrenaline in dogs and cats (12) and to the prolongation of toxic immobility in lizards by adrenaline (9). Possibly the slow adsorption from the peritoneal cavity provides the equivalent of the slow perfusion of adrenaline that Rothballer (13) reports is very effective in inducing adrenaline stupor.

SUMMARY

The following facts arise from this investigation:

(*i*) The loss of the methoxy group in the 5 position of mescaline is responsible for some 50 per cent. loss of activity *as measured by this test.*

(*ii*) The replacement of the 4-methoxy group by a hydroxyl group eliminates activity and by a benzyloxy group increases activity.

(*iii*) Adrenaline has a marked behavioural effect administered in high dosage by the i.p. route.

(*iv*) Dopamine, in doses up to 40 mg./kg. has very little behavioural effect.

(*v*) 5-hydroxy-dopamine has a moderate degree of activity.

(*vi*) It is possible that results (*iii*)–(*v*) may not be due solely to the associated hypertension. Various metabolites and derivatives of adrenaline were tested in a dosage equal to or above that that might be expected to be formed from the highest dose of adrenaline used. These were, however, all quite inactive.

It would be of great interest to extend this investigation by using more compounds in this series and by testing them with other methods. The final test for any alleged hallucinogenic compound must be, of course, in human volunteers, as one cannot argue directly from rat to man. However, the results presented here give an indication of the range of response that may be expected. The extent of the present investigation was limited by the availability of compounds.

Acknowledgments

We are greatly indebted to Mr. J. Lazarz for his technical assistance and to the following companies for their generous gift of compounds: Hoffman-La Roche Inc. for IV and V (as hydrochlorides) and VII (as hydrobromide); to Ciba pharmaceuticals, the William S. Merrell Company and Abbott Laboratories for II (as hydrochloride) and to Ciba for dopamine in addition (as hydrochloride). Dr. Oscar Resnick very kindly gave us metanephrine (as hydrochloride) and vanillyl-mandelic acid. We are also most grateful to Dr. Jack Bergen for the loan of facilities.

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THE CONCEPT OF THE PSYCHOPATH*

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IN their evidence to the recent Royal Commission on the Law Relating to Mental Illness and Mental Deficiency the R.M.P.A. stated the problem of the psychopath in terms of delinquent or otherwise anti-social behaviour. After eliminating cases where such behaviour resulted from well-recognized forms of mental illness or defect, from psychoneurosis or organic disease or injury, their Memorandum went on to say that there remained a group of patients "whose daily behaviour shows a want of social responsibility and of consideration for others, of prudence and foresight and of ability to act in their own best interests. Their persistent anti-social mode of conduct may include inefficiency and lack of interest in any form of occupation; pathological lying, swindling and slandering; alcoholism and drug addiction, sexual offences, and violent actions with little motivation and an entire absence of self-restraint, which may go as far as homicide. Punishment, or the threat of punishment, influences their behaviour only momentarily and its more lasting effect is to intensify their vindictiveness and anti-social attitude."

This description in itself raises many issues—for example, it deals with the particular way in which such people act and not with their motivation. The relevance of the distinction between what one does and why one does it is an issue which will be referred to later. For the moment one comment will suffice, viz. that the terms used are—"conduct", not "illness" and "misbehaviour", not "suffering". There is no way, except for the fact that the word "patients" is used, of telling that this description refers to a medical condition.

This introduces the first and the major consideration—that of the status of the psychopath as a medical problem.

The question of the medical status of the psychopath is raised while fully acknowledging the virtue of the doctors' inherent sympathy and desire to help all the cases that are presented to them. The intention is not to be concerned with the doctor's limitations either personally, professionally or technically but to raise the *social* issues which follow from the above description of the psychopath—issues which, it can be argued, are incompatible with the clinical frame of reference.

To do this it is necessary to go further and to consider a still more basic question, viz. the legitimacy or propriety of including emotional difficulties within the range of medical intervention. Emotional difficulties have in fact *become* the concern of the psychiatrist and a review of the ways in which this present position has been reached is offered in order to illuminate the particular problem of the medical status of the psychopath.

Emotional problems, as we use the term, can refer either to problems of experiencing or expressing emotions or to problems of another kind which are regarded as being determined by emotional factors. The patient can approach the physician complaining of emotional problems, hoping to profit by the physician's sagacity, but not strictly in his traditional role as a doctor, i.e. the approach would be outside a strict clinical frame of reference. The physician might respond with personal advice, i.e. on a "man to man" basis, or he might translate the problem into clinical terms by recommending sedatives, rest, holidays, etc. Functional illnesses are in themselves an expression of emotional problems and they are also ways in which patients carry their emotional difficulties to doctors in an indirect or disguised form.

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* Read at the Annual Meeting of the Royal Medico-Psychological Association in Glasgow, July 16, 1959.

Before Freud, the accepted way of presenting an emotional problem to a doctor was in a strictly somatic form and the expected response on the doctor's part was in terms of the conventional clinico-pathological method. The symptoms were viewed not as an emotional problem but as being occasioned by some as yet undetected physiological or pathological process. The sickness and symptoms lay conveniently within a bodily frame of reference—trembling, headache, paralysis, anaesthesia, fainting. What Freud did was to present a new clinical frame of reference in which symptoms became symbols, the lesions were emotions and not physiological processes, and the clinical dimension was the history of the patient and not the history of the illness.

This, properly speaking, was a new clinical pathology but it became much more. Illness was seen at a new level and in fact a new kind of illness was created—emotional disorder. Inhibitions, repressions and the like, which were concepts belonging to underlying pathology, became themselves diseases and symptoms. Because patients could experience their pathology by a more or less healthy introspection, they came complaining not of the symptoms but of the basic processes themselves, and this kind of approach by the patient was accepted by the doctor and built in to medicine. It is as if the patient, instead of recounting his malaise and fatigue, complained of vitamin deficiency or, to make the analogy extreme, he complained of something like electrolyte imbalance rather than the appropriate bodily symptoms from which the existence of this imbalance could be inferred by the doctor.

The other trend in the development of medical acceptance of emotional difficulties stems from the way in which psychodynamic formulations were generalized, made comprehensive and applied to all human motivation and development and not just to the special subgroup of those who are psychologically sick. Academically, psychoanalysis spread to psychology, to anthropology, sociology and directly and indirectly to everyday life. Again this emotional pathology was applied, like a clinical pathology, to areas in which relationships with people were the dynamic—to wars, industrial disputes, spanking children, fine arts and of course to sexual behaviour. Terms like "social pathology", "sick society", reflected this transmutation of a clinical to a social approach. Words like "anxiety", "guilt", "masochism", "complexes", "neurotic", "psychotic", became current usage divorced from their clinical context. Groups and individuals turned to psychiatry for guidance, not in the consulting room but in magazines, books, radio and television. Again, what they discovered in themselves was emotional maladjustment—that one-time pathological concept now masquerading as a symptom. But it had to have a content—hating people, misbehaving and acting out, all because of emotional maladjustment thought of as being occasioned by adverse early experiences. From this originally metaphorical application of pathological concepts outside the consulting room certain assumptions are fed back into the clinical situation. One of these assumptions, promoted very largely by sociological students of psychiatry, leads to the assertion that the psychoneurotic and the psychopath are fellow sufferers with the same pathology.

It is at this point that medicine and morality get entangled around the ideal of the mentally healthy person. He is a person who has escaped the pitfalls which the neurotic's biography reveals or who has had these unfortunate experiences restructured by therapeutic or beneficent influences. He is well-adjusted, tolerates interpersonal stress and does not clash with society. The mentally sick person on the other hand is by psychopathological definition not well-adjusted and correspondingly less able to conform to social standards of conduct.

In a sense the mentally sick person suffers because he cannot conform. He does not feel or act like other people. It is of this that he complains or is complained about and may be the reason why he seeks medical help. He suffers or causes suffering because of a clash with social norms or values. However, in dealing with mental illness the psychiatrist can translate the complaint into a clinical frame of reference, i.e. away from the social, by attending to other aspects of the illness and elaborating these as primary—dwelling, for example, on formal disorders of mood or thought. By his conventional approach he is able to formulate the illness as a psychological syndrome independent of social considerations and sometimes even as a disease independent of biographical considerations.

This answers the general question about the propriety of accepting emotional disorders as medical. They are medical because they can be understood by the conventional clinical approach.

The more specific question of how proper it is for medicine to deal with psychopaths can now be considered. The issue here is more in doubt because the psychopath who complains of antisocial behaviour and is complained about on these same grounds does not permit any translation from the social to the clinical spheres and therefore the clinico-pathological convention does not operate.

In order to develop this latter point a statement of what is meant by the clinico-pathological convention is required. This term is used to describe the formal mode of thinking by which all doctors operate, whatever their medical discipline, and in which the symptoms reported by the patient are related to the signs observed by the doctor and to a known pathology. This leads to the formulation of a diagnosis and of a prognosis and to the prescription of a treatment. This conveys the essence of the convention but is an over-simplification. It is not just a one-way process in which symptoms lead to pathology and thence to treatment but it involves reciprocation and feedback at all stages—the recognition of the signs of pathology may for example lead to a re-investigation of symptoms and the response to treatment to a reassessment of the pathology.

An essential requirement of this method is the possibility of translating phenomena from one frame of reference to another. This applies when symptoms have to be understood in terms of their pathology, and pathology in terms of possibilities of treatment. It also applies when the significance of symptoms is determined by moving from the physical to the psychological or in the other direction.

In the case of the psychopath who presents with antisocial conduct the difficulty is to translate his "symptom" into another frame of reference. If we merely say that he behaves antisocially and that therefore he must be socially sick, we get no further than a statement of the obvious. The clinical convention is thwarted because there is no alternative frame of reference to the social into which his antisocial symptoms will fit. In passing it should be mentioned that there are some possibilities for related pathology such as the faulty time sense or lack of appreciation of time which has been observed in psychopaths and which may in time provide a basis for a clinical approach.

On the other hand it might be argued that, given antisocial conduct in one form, it is possible to predict that the individual will be antisocial in other forms or in other directions and further that the ability to make such a prediction stems from an act of clinical perception of the same nature as a medical diagnosis. This is however no more than to re-state the terms of the description of the psychopath given at the beginning, viz. that the antisocial mode of conduct is widespread and persistent. There is still no process of translation by which the antisocial disturbance can be unequivocably related to a pathology. The temptation is to ignore the requirements of the clinico-pathological convention that symptoms should be present outwith the social frame of reference and to assume instead that, because psychoneurotic patients also have social symptoms, we can take for granted a similar psychopathology for psychopaths.

The kind of approach which starts from a statement of the dissatisfactions with the term "psychopath" and seeks to replace it by terms such as "claustration" (Gayral, 1954), "sociopath", "anethopath" (Karpman, 1949), or which crystallizes the pathology in terms such as "affect starvation", "poverty of affectivity" or even "oligothymia" (Davidson, 1957), by the same token does not make the concept any more clinical by emphasizing the socially determined nature of the condition.

The "constitutional" approach might seem on the face of it to be more clinical than the psychodynamic because it postulates characteristics which have developmental and biological implications apparently independent of social values. This again is likely to be false if the innate origins of socially unacceptable behaviour are merely inferences and if such conclusions are arrived at on the basis of descriptions couched in terms of social acceptability. This is so with Schneider (1958) who is well aware of the conceptual difficulties involved in the term "psychopath". He asserts that psychopathy lies in the degree to which the abnormality of personality afflicts the individual, and not the amount of social friction which may be engendered around him. Psychopathic personalities are no more than abnormal personalities and the psychopath who brings suffering on the community does so only because he has an abnormal personality which deviates from the norm quite apart from social consequence.

This formulation would seem sufficient to counter the objection raised above that psychopathy does not permit a non-social frame of reference for symptoms. However, Schneider goes on to remove the condition from the clinical convention altogether. "To call the social nuisance or misfit sick or ill is to use the word 'ill' as a metaphor and to mean forms of behaviour which the group will not tolerate" (p. 8). Further, his typology with its variations of the psychopathic personality is not to be confused with diagnosis. Schneider says that to describe a person as a depressive psychopath means nothing more than that he is a man of this sort. "The human personality cannot be labelled diagnostically as we label mental or physical symptoms. Human qualities may be indicated, emphasized and perhaps isolated as distinguishing characteristics but this is not committal to some diagnostic statement about a symptom." (p. 51). "There is however a tendency for description by psychopathic type to be accepted as a description of the other aspect, the personality *in toto*, or at any rate of its essential characteristics—a kind of psychic diagnosis" (p. 52).

The term "psychopath" to Schneider characterizes personality and not illness. Irrespective of whether it is sound theory or not such a distinction does not have much practical worth when the psychopath is encountered by the clinician whose orientation leads him to take a more active and interventionist role than the statement about personality would warrant.

In Schneider's defence it must be stated that the passages quoted are inconsistent with his overall approach which is definitely clinical. The fact that he is led into such difficulties and that his claim to avoid value or judgmental issues is not borne out by the descriptions in the illustrative section of his book confirms the precarious clinical status of the psychopathic state. Even Schneider's approach which avoids psychopathology leads back to the same dilemma for the clinician.

Again, when physiological criteria are considered it would seem possible to operate away from social factors in terms of an EEG abnormality, for example. Numerous authors have investigated patients diagnosed as psychopaths or criminals considered to be psychopathic by means of electroencephalography. These studies reveal the presence of an abnormal record in varying proportions of the group—but roughly in about 60 per cent.—the abnormality generally being of slow activity, between 5 and 7 cycles per second. No specific EEG pattern which allows us to identify psychopathy is found; instead there is a variety of patterns all of which occur also in a proportion of the normal population (Maughs, 1955). The discovery of this kind of abnormality has led to various formulations:

1. That of specific pathophysiology with possible relationships to diseases such as epilepsy or to sequelae of diseases such as encephalitis.
2. Delayed maturation, cortical immaturity and non-structural alteration in brain function.
3. Related dysrhythmias within families as evidence of a genetic basis for the condition.

This approach can also lead to the compromise view that psychogenic or situational factors may still operate to produce psychopathy but only in an individual whose threshold for or predisposition to antisocial conduct is low because of an "organic component" (e.g. Knott and Gottlieb, 1944; Silverman, 1949). However, the problem remains one of interpretation and of defining which features give the EEG abnormality their significance. Again the only criterion appears to be antisocial behaviour.

The argument so far has been destructive, viz. that the psychopath is a moralist's and not a clinician's diagnosis and that the clinical approach cannot operate. An analogy may permit a more constructive formulation. In the past many comparisons have been made between the psychopath and the mentally defective individual (e.g. Henderson, 1951). It might be more profitable to compare not the individual but the conditions. "Mental defect" describes a state or condition capable of being produced by a number of diseases, anomalies, or no disease at all, and which is a social, legal or administrative concept. Like "psychopathic personality" this term in the past has created confusion between social and clinical criteria and may in fact still do so. Clinical work on mental defect eventually developed away from the social aspects because it was possible to make a biological interpretation on the basis of the known distribution and inheritance of intelligence as a human characteristic. This led to a distinction between subcultural and pathological and thus to a knowledge of what was primary and secondary or what was inherited and what was acquired in the condition. Further refinement has led to the present phase in which one begins to see the separating out of specific diseases and pathologies for specific instances of the condition.

Work on mental defect started from the establishment of an administrative or legal concept which allowed patients with the condition to come under medical care in large enough groups to permit comparative and epidemiological studies to be undertaken. In this connection the new administrative arrangements for the care of psychopaths may in the future have a great deal of influence on whether or not the clinical aspects of the condition are revealed. Ideally one should have a parameter akin to the distribution of individual differences in intelligence to provide a biological parallel to the social or conforming dimensions of the problem. One has to be speculative here but it may well be that the recently developed ethological concepts of instinct will provide a new approach to development and maturation.

Perhaps the stage has not been reached when clinical or laboratory work of a scientific nature is ready to be undertaken with respect to the psychopath. To pursue the analogy with mental defect, it may be that we are still at the same stage with respect to psychopathic personalities that the philosophers and pedants were when faced with problems raised by the Wild Boy of Aveyron and that some basic change of attitude, both social and scientific, is necessary before clinical work can be developed.*

This leaves the clinical psychiatrist for the moment with the difficulty of operating at two levels with respect to the psychopath: (*a*) as a clinician determined to help the individual patient who presents or is presented to him; (*b*) as a creator of a new kind of morality concerned with the motives for conduct and the basis of individual responsibility.

It is important that these roles should not be confused. This again is difficult because clinical judgment has to be reconciled with social responsibility. As a citizen the psychiatrist is concerned with acts and their rightness or wrongness independently of their motives; in his consulting room he is primarily concerned with motives.

ACKNOWLEDGMENTS

Achnowledgments are due to Professor T. Ferguson Rodger for his help and encouragement.

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* In this respect it is interesting to note that Kahn (1949) talks about the psychopath as an evolutionary anachronism and Karpman (1949) has discussed psychopathy as a form of social parasitism, using this term in its biological sense.

† A similar discussion to the above is to be found in Barbara Wootton's *Social Science and Social Pathology*, 1959. Allen & Unwin.

TEMPORAL LOBECTOMY FOR PSYCHOMOTOR EPILEPSY

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SURGICAL removal of the temporal lobe is becoming an established therapeutic procedure in the treatment of focal epilepsy arising in one or other of the temporal lobes and good results in the control of otherwise intractable seizures have been widely reported (e.g. Falconer *et al.*, 5; Picaza and Guma, 18). Indeed, with increasing experience of anterior temporal lobectomy and delineation of the indications for operation, even greater success may be anticipated (Hill, 9; Rasmussen and Jasper, 19).

Beside fits many patients suffering from temporal lobe epilepsy exhibit psychiatric abnormalities of greater or lesser extent. These may take the form of acute disturbances of behaviour (e.g. aggressive conduct or psychotic episodes) often directly related to epileptic activity, or of sustained neurotic states but little influenced by the occurrence or the frequency of the seizures. In many cases, however, the mental abnormality appears more related to a disorganization of cerebral functioning occasioned by overt or subclinical epileptic discharges or to the abnormal life stresses to which the epileptic patient is subjected than to any concomitant irreversible cerebral pathology or intrinsic personality deficit. In such cases considerable psychiatric improvement may follow the relief of epilepsy by surgery.

Various authors have noted personality improvement after temporal lobectomy for temporal lobe epilepsy. Thus Guillaume *et al.* (8) reported improvement in 15 of 18 patients with "character disorders", Alajouanine *et al.* (1) in the majority of 15 patients with "mental disturbance", and Bailey *et al.* (2) in 45 of 65 patients, half of whom had previously shown "psychosis or severe personality disturbance". Liddell and Northfield (13) have also described considerable improvement in intellectual capacity following operation in two patients with a clinical state resembling mental deficiency but associated with frequent temporal lobe epileptic discharges.

Hill, Pond, Mitchell and Falconer (10) have previously reported personality changes and social improvement with the seizure control obtained after temporal lobectomy in 18 of 26 patients submitted to surgery at the Guy's-Maudsley Neurosurgical Unit. The present study of an extended series of 72 consecutive cases followed up intensively for from one to six years suggests that:

(*i*) Improvement in social and personal adjustment after operation is usual, and although related to seizure control may occur even if this is incomplete.

(*ii*) This improvement is usually progressive and may continue for a considerable period after operation before its final extent is reached.

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(*iii*) Active psychiatric after-care including psychotherapeutically orientated out-patient support, early in-patient treatment during acute relapses, co-ordinated occupational rehabilitation, social agency aid, etc., is often important in obtaining the maximum level of social improvement possible.

CASE MATERIAL

Seventy-two patients consecutively subjected to anterior temporal lobectomy for epileptic seizures uncontrolled by an adequate anticonvulsant drug regime were followed up for from one to six years (mean period of follow-up=3·9 years). The programme included regular out-patient attendances as well as visits by the author to patients at home, at work, or in hospitals, etc. Where post-operative psychiatric treatment was needed this was, whenever possible, arranged at the Neurosurgical Unit or in one of the psychiatric wards of the Maudsley Hospital, so that continuity of psychiatric management was provided for. Four patients who left the country at varying periods after operation were subsequently followed by letters from the patient, the family and the medical attendant. Three others who died between one and three years after operation are mentioned separately in the "final assessments" although included in the pre-operative assessments.

Epileptic patients in whom preliminary investigations disclosed a cerebral space-occupying lesion were not included in this series but were regarded as "tumour cases". In spite of this screening a proportion of the cases were found at operation to have small tumours or focal lesions in or adjacent to the temporal lobe (Cavanagh, 3; Falconer and Cavanagh, 4). In no case has there yet been any clinical evidence of tumour recurrence although this must remain a possibility in a few instances. The patients ranged in age at time of operation from 11 to 56 years, and the mean age of onset, duration of epilepsy, intelligence quotient, and the pathological findings at operation are contained in Table I.

TABLE I

Relationship Between Personality Disorder and Epilepsy, I.Q. and Pathology

					Pathology		
		Epilepsy		Mean Full Scale I.Q.	Mesial Temporal Lobe Gliosis		
Personality	No.	Mean Age of Onset (years)	Mean Duration (years)	Before Operation	With A.H.S.*	Without A.H.S.*	Discrete Focal Lesions
Aggressive ..	20	6·4±1·1	12·1±1·3	88·1±2·4	12	7	1
Psychotic ..	7	14·9±2·9	18·7±3·3	112·6±5·4	4	3	0
Neurotic ..	14	14·5±1·9	17·0±2·5	98·6±3·2	6	5	3
Deterioration	3	35·3	12·3	—	0	0	3
Defective ..	4	4·0	8·0	—	1	1	2
Marginal ..	17 } 24	20·9±3·1	11·5±1·8	106·8±3·7	11	4	9
Normal ..	7						
All cases ..	72	14·7±1·4	13·5±0·9	100·4±2·0	34	20	18

* A.H.S.=Ammon's horn sclerosis.

Sixty-five of the 72 patients in the series were found to have clinical psychiatric abnormalities in addition to epileptic seizures before operation (Table I). This incidence (no less than 85 per cent. even if 4 patients of high grade defective intelligence are excluded) is in accord with the findings of Alajouanine *et al.* (1), who reported mental abnormality in 18 of 22 cases submitted to temporal lobectomy, but is higher than that encountered by some other authors (Guillaume *et al.*, 8; Bailey *et al.*, 2). The frequency of associated mental disturbance may be due in part to the fact that many patients in our series were referred from psychiatric sources and cases were not necessarily excluded from operation on personality grounds. It is also possible that routine extensive psychiatric examination sometimes disclosed abnormality in patients whose symptomatology was dominated by their epilepsy and in whom it might otherwise have escaped notice. The value of a full pre-operative personality study was considerable in predicting post-operative problems and instituting supportive measures early after operation.

PRE-OPERATIVE PSYCHIATRIC DISORDER

The majority of our patients showed severe psychiatric disturbance in addition to fits and this often constituted a much greater disability to the patient than their epilepsy. The individual range of symptoms varied considerably and almost every type of psychiatric syndrome was encountered.

On the basis of the predominant disturbance present the cases were divided into 7 groups:

Severe aggressive conduct disorder	20 cases (28 per cent.)
Psychosis or psychotic episodes	7 cases (10 per cent.)
Neurotic states	14 cases (19 per cent.)
Personality deterioration of late onset	3 cases (4 per cent.)
High-grade mental defect	4 cases (5 per cent.)
Marginal disorders	17 cases (24 per cent.)
Normal personality	7 cases (10 per cent.)

Only seven patients could be described as having "normal personalities", whilst 17 cases included in the "marginal" group showed definite features of neurotic or psychopathic disorder, but with less severity than those allocated to the other groups.

This grouping differs somewhat in detail from the descriptive classifications of pre-operative personality disorder used in previous communications on temporal lobe epilepsy from the Guy's-Maudsley Unit and aims at indicating severity as well as nosology.

The surgical technique employed allowed detailed histological examination of the removed temporal lobe in all cases and Table I indicates the pathological findings in the various personality groups. Whilst there was a tendency for patients with more severe sclerosis of the mesial temporal structures (including Ammon's horn) to show more severe mental disturbance and for those with discrete focal lesions to have more normal personalities, there was no statistically significant correlation between pathology and type of personality disorder (excluding the deteriorated and defective groups in Table I, $\chi^2=10\cdot 14$: not significant beyond the 10 per cent. level).

Aggressive Group: A large percentage of patients with temporal lobe epilepsy show undue aggressivity. This varies from irritability of trait level to violent or even homicidal conduct. In 20 patients aggression dominated the clinical picture, and indeed in these patients neurotic or other personality features were often singularly lacking. None showed true psychotic symptoms in addition to the aggression.

It was characterized by unpredictable explosive outbursts in response to minor or trivially frustrating situations, and was often related to epileptic seizures either directly (occurring pre- or post-ictally) or indirectly (affected by changes in fit frequency). However, in all the patients in this group there was clearly an aggressive personality disorder and the behaviour was not solely an "epileptic equivalent". In some the aggressive conduct, although ictally related, was remarkably selectively directed at certain individuals, usually parents or siblings. Thus a patient whose conduct was violent in the home might show little disturbance in other social settings, even though fits occurred anywhere. Whilst in most cases the aggressivity followed the onset of seizures by months or even years, occasionally severe aggressive conduct predated overt fits; in one instance by over 5 years. Many of these patients had acquired the label of "epileptic psychopath", as their outbursts brought them into frequent conflict with society. This was seldom justified, as there was often little evidence of intrinsic psychopathic traits in other fields of conduct and the rapidity of personality recovery after seizure control did not accord with the usual concepts of psychopathy.

All but one of the patients included in this group had been excluded from school, admitted to hospital or institutions, or had appeared in a police court because of aggressive behaviour. The remaining patient had made violent attacks on members of his family.

The aggressive patients differed significantly from those with normal or less severely disturbed personalities (the marginal/normal group) in having an earlier mean age of onset of epilepsy and a lower intelligence level. In all but one overt seizures had commenced before the age of 13 years, whilst the mean full scale I.Q. for the group was over 18 points lower than that for the marginal/normal group ($t=4\cdot415$, significant beyond the ·1 per cent. level). The aggressive group also contained a greater proportion of patients with severe mesial temporal lobe sclerosis and of patients from lower social class homes than did the series as a whole. They were nearly all socially maladjusted to a severe degree, and the earlier age at which this group of patients came to operation (mean age at operation 18·4 years, as opposed to 28·2 years for the whole series) seems partly a measure of the urgent need for treatment.

Psychotic Group: Seven patients in our series had, before operation, suffered from acute psychotic states, usually requiring admission to hospital under certificate. In 4 cases these took the form of psychotic depression with paranoid delusions lasting a few days or a few weeks, with virtual recovery between episodes. The psychotic states seemed related to epileptic activity in that they followed an increase in fit frequency in 3 patients whilst the fourth was subject to increasingly severe psychotic depression for some days until this was relieved by the occurrence of one or more major seizures. This patient had learned to relieve his depressive attacks by temporarily stopping his drugs. In 2 cases there was a history of acute "schizophrenic-like" states. Both had recovered from the acute phase but still retained symptoms; one maintained fixed ideas of religious conversion, the other remained suspicious and anxious. Finally one patient had been certified and had been in a mental hospital with typical paranoid schizophrenia for a year before operation.

All these patients had suffered from fits for many years before the onset of psychotic symptoms although in most instances overt seizures had not commenced until after childhood. Surprisingly the mean I.Q. of this group was higher than any of the others, although temporal lobe gliosis was present in each case.

Neurotic Group: Fourteen of the 72 patients presented clinical neurotic states of a kind which would merit treatment in their own right in psychiatric practice. There was no characteristic pattern, and cases included obsessional, phobic, anxiety, depressive, hysterical and diffuse neurotic syndromes. There was rarely any direct relationship between seizures and individual symptoms, although exacerbation of the neurotic state sometimes followed periods of increased fit frequency. There was more frequently evidence of psychopathological stress or of constitutional predisposition to psychiatric illness than in the previous two groups, and many of these patients were obviously more disabled by the neurosis than by their epilepsy. In over half the cases epileptic seizures had commenced shortly after puberty and in all but two between the ages of 11 and 22 years (mean age of onset $14{\cdot}5 \pm 1{\cdot}9$ years).

Personality Deterioration: Three patients who showed personality deterioration of late onset without dementia could not be allotted to any of our other categories. The picture was of social deterioration characterized by irritability, depression, poor concentration and memory, deterioration of personal habits, etc., but without any evidence of intellectual deficit on psychological tests. In one patient progressive character change followed a head injury, another was a chronic alcoholic, whilst in the third case a small unsuspected cerebral tumour was disclosed at operation. Only the tumour case was benefited by operation. The other two had been operated on early in the series and would probably not be selected on present criteria.

Defective Intelligence: Four patients were of high-grade defective intelligence (I.Q. 50 to 68) and were aged between 13 and 19 years of age at operation. Three in addition showed behaviour disorders of an immature defective type. Intellectual capacity was uninfluenced by lobectomy although in 3 both the psychiatric status and the epilepsy were improved by operation.

Marginal/Normal Group: Only 7 patients (under 10 per cent. of the series) were found to have a "normal personality" in spite of their epilepsy, whilst 14 others, the "marginal group", showed psychiatric abnormality less severe than those assigned to the other groups. Generally the "marginal" patients suffered from deficits of personality adjustment at trait level with or without recognized psychiatric symptoms, but had not received treatment for psychological illness. Some were best described as "immature inadequate personalities" with or without "latent homosexuality component", others showed paranoid personality traits or milder instability of a psychopathic type, whilst patients with less severe phobic anxiety states or with neurotic traits were also included. In these cases constitutional and environmental factors seemed important. Many lived in overprotective or hostile family circles, or else came from families in which neurotic illness was prominent. There was little difference between the "normal" and "marginal" groups in terms of epileptic pattern, pathology, mean I.Q., etc., and so they have been combined in the tables.

IMPROVEMENT IN PSYCHIATRIC STATUS AND SOCIAL ADJUSTMENT FOLLOWING OPERATION

Considerable improvement in psychiatric status followed operation in 41 (57 per cent.) of the 72 patients studied and this amounted to recovery in 18. A further 13 cases showed "some improvement" during the period of survey. Over the same period 39 patients (54 per cent.) had been relieved of their epilepsy, or virtually so, whilst in a further 13 (18 per cent) the seizure frequency had been reduced by half or more.

There was a close but by no means absolute relationship between fit control and psychiatric improvement (Table II). An overall correlation coefficient of $+\cdot602$ ($p<\cdot001$) was found between individual ratings of seizure reduction and of personality improvement. This relationship was closest in the group of patients with aggressive personality disorders ($r=+\cdot714$; $p<\cdot001$) but in the neurotic group no significant correlation could be demonstrated ($r=+\cdot305$; $p>\cdot1$). While in a few cases dramatic psychiatric improvement was apparent soon after operation, the more usual pattern was of delayed or of slowly progressive improvement which did not reach its final extent for months or even years.

TABLE II

Correlation Between Personality Improvement and Seizure Control
(62 patients with pre-operative psychiatric disorder)

Seizure Control			Personality Improvement		
Rating *	Fits	No.	Rating	Personality	No.
5	No fits	32	5	Recovered	18
4	1 or 2 per year	7	4	Very much improved ..	12
3	50 per cent. reduction ..	13	3	Improved	11
2	25 per cent. reduction ..	2	2	Some improvement ..	13
1	No change	8	1	No change	8

Correlation Coefficients

All Cases	$N=62$	$r=+\cdot602$	$p=<\cdot001$
Aggressive Group	$N=19$	$r=+\cdot714$	$p=<\cdot001$
Neurotic Group	$N=14$	$r=+\cdot305$	$p=>\cdot1$ (N.S.)

* After Penfield and Steelman (17).

Universal criteria of psychiatric improvement were difficult to formulate, since the initial disorder varied considerably from one patient to another. In order to gain an impression of the recovery pattern of the series as a whole each patient was rated before and at intervals after operation against defined criteria on 4-point rating scales of "work capacity", "need for hospital treatment", "level of relationship with family" and "social activity" (Table III). A patient who worked full time at a normal occupation and missed less than 4 weeks per year through indisposition was rated 4 for work capacity. If he worked in a sheltered occupation or below his intellectual capacity, or missed up to 8 weeks during the year he was rated 3. Part-time work or repeated absences or frequent changes rated 2, and less than 3 months work per year rated 1. Parallel ratings based on school performance or household capacity were used for the few children and housewives in the series. The scales for the 3 other factors were similarly constructed and applied to all patients. The mean rating achieved by a particular patient appeared to be some index of the level of social adjustment at a particular time. Table III shows the pattern of improvement after operation. This was progressive for some two years but thereafter little increase occurred in the proportion of patients who achieved good social adjustment. This period of psychiatric recovery was often stormy. Many patients needed active psychiatric treatment and almost one-third were temporarily re-admitted to hospital for this during the two years following surgery. *However, since permanent improvement was eventually obtained in the majority of cases the need for further psychiatric treatment after operation should*

TABLE III

Social Adjustment Before and After Operation

Rating		Before Operation	6 Months Post-operation	1 Year Post-operation	2 Years Post-operation	3 Years Post-operation	Level of Adjustment
Work Capacity	1	24	22	13	8	6	Little or no work.
	2	13	7	13	7	5	Intermittent or part work.
	3	20} 49%	19} 60%	20} 64%	20} 75%	19} 78%	Full work (reduced capacity).
	4	15}	24}	26}	25}	19}	Full work (full capacity).
Hospital Treatments	1	8	6	5	3	2	Mainly I.P. treatment.
	2	22	14	13	5	4	Repeated admission.
	3	10} 58%	5} 72%	7} 75%	11} 87%	5} 88%	One brief admission or regular O.P. treatment.
	4	32}	47}	47}	41}	38}	No treatment or occasional O.P. treatment.
Family Relationships	1	8	3	5	5	2	Disturbance causing separation.
	2	25	20	13	7	6	Disturbed, but united.
	3	26} 54%	30} 68%	32} 75%	24} 80%	20} 84%	Minimal disturbance.
	4	13}	19}	22}	24}	21}	Good relationship.
Social Activity	1	8	3	2	2	4	Gross disturbance.
	2	34	22	23	17	13	Much reduced sociability.
	3	21} 42%	31} 65%	27} 65%	22} 68%	14} 66%	Slight restriction.
	4	9}	16}	20}	19}	18}	Full sociability.
No. in Group:		72	72	72	60 (excluding 1 died)	49 (excluding 3 died)	

not be regarded as a failure of therapy but as an essential part of post-operative "psychiatric after-care".

Table IV indicates the eventual improvement in social adjustment. This was most striking in those patients with severe aggressive personality disorders. Nineteen of 20 such cases rated poor social adjustment before operation compared with only 5 out of 19 at the end of the follow-up period. Personality improvement nearly always followed if the fits were controlled, whilst in 3 cases recurrence of seizures was followed after a period of time by further aggressive conduct disorder, which again resolved when the fits were once more controlled by anticonvulsants or subsided spontaneously. Similar improvement occurred in 3 of 6 patients with a history of psychotic symptoms.

TABLE IV

Improvement in Social Adjustment Following Operation

		Socially Well Adjusted (Rating 3 or 4)	
Personality	No.	Before Operation	Final Assessment
Aggressive*	20	1 (5%)	14 (73%)
Psychotic*	7	1 (14%)	4 (66%)
Neurotic	14	5 (36%)	10 (71%)
Marginal normal	24	19 (79%)	23 (96%)
All cases	65	26 (40%)	51 (81%)

* One patient in each of these groups died during follow-up period.

In those patients with neurotic states before operation, on the other hand, social improvement was less apparent and when it occurred usually delayed. It rarely followed directly upon seizure control and was perhaps more related to further psychiatric treatment, to rehabilitation therapy, to removal of the stigma of epilepsy, etc. Nevertheless 5 patients in the group showed considerable improvement whilst in only one instance did the social status deteriorate. Neurotic symptoms are not necessarily a contraindication to lobectomy for temporal lobe epilepsy, although patients with long-standing hysterical personalities rarely improve. Assessment of the patient's total personality pattern rather than of individual symptoms alone will indicate whether improvement may be anticipated or not.

Some Factors Influencing Disability and Recovery

Before considering our experiences of the post-operative psychiatric management of patients after temporal lobectomy three aspects of the problem may be singled out for comment.

(i) *Epileptic Disability:* The actual occurrence of seizures may play but a small part in the epileptic patient's "total disability". Gordon and Russell (7) studied 400 adult epileptics attending the out-patient department of a neurological hospital (National Hospital, Queen Square, London). Under 10 per cent. were totally unemployed, although the vast majority of those working suffered from major convulsive fits. Those patients who were unemployed did not differ from the others in the severity of their epilepsy—but were of somewhat lower intelligence and the authors concluded that "it was this factor and sometimes disorders of personality that more frequently prevented them from obtaining work than the presence of such a disability as epilepsy".

Kennedy and Seccombe (11) studied 100 patients consecutively referred to the epileptic out-patient clinic at a psychiatric hospital (Maudsley Hospital, London). Three-quarters of the 82 patients who in fact proved to be epileptic had in addition some personality disturbance and 38 per cent. of the "working population" of this group had a poor work record (unemployed for more than 3 of the previous 10 years). These authors also found that poor work record was significantly related to severity of personality disorder and to lower I.Q. but not to the severity of their epileptic seizures.

Earl Walker (21) in a 10-year follow-up of wartime post-traumatic epileptics found that of 102 patients who had become seizure free (most for over 5 years) only 50 per cent. were gainfully employed. Severe neurological deficit or continued fits had little effect on the proportion who were socially adjusted. Many suffered from "a much more complex disability than hemiplegia or epilepsy" and such defects alone "did not account for their failure to return to a normal existence".

Control of the epileptic seizures alone may be but one factor, albeit an important one, in the treatment of the epileptic patient's total disability.

(ii) *Recovery from Epilepsy:* Epilepsy is stressful to an individual, not only because of the dangers, injuries, and physiological disturbances concomitant upon the ictus but also because of the additional personal and social stresses to which the epileptic is subjected. Minor seizures with little objective evidence of their occurrence may excite little notice, but a person who falls, convulses, or suffers an automatism is not easily acceptable to many social groups. Employers are at first reluctant to offer jobs; workmates may be hostile and acquaintances afraid of developing friendships. Understandably many epileptics are reluctant to disclose their illness to prospective employers or friends but may be constantly afraid lest a fit occurs to reveal their secret. A large part of normal social activity may be denied the epileptic and some of those whose seizures commenced in childhood may emerge into adult life without any of the normal social experiences of adolescence. The patient's family reacting to this often develops an overprotective attitude and so adds to the patient's isolation. The prospect of being rendered senseless in dangerous situations, of "losing control", of automatic behaviour for which the patient has no memory, of incontinence in social company, etc., invest the epileptic seizure with an intensely personal and stressful meaning. It is neither surprising that neurotic patterns of adjustment so often accompany epilepsy, nor that conflict symptoms are closely bound up with the ictus at symbolic as well as physiological levels. The ictus becomes a scapegoat for all personal difficulties —and yet at the same time it may subserve an egosyntonic function by permitting the paroxysmal discharge of mounting psychic tension. Freud (6) suggested that "the epileptic discharge places itself at the disposal of the neurosis, the essence of which is to get rid by somatic means of masses of stimuli which it can't deal with psychically". Control of the seizures does not automatically abolish neurotic patterns of adjustment to life. The development of alternative mechanisms for dealing with intrinsic anxiety may be slow and painful. Indeed patients are sometimes aware of this and complain of constant tension, whereas previously they were at least subject to occasional post-ictal relief. The tenor of the patient's readjustment to "life without epilepsy" is set in the early post-operative period and psychotherapeutic help then may be invaluable.

(iii) *Psychological Changes Following Temporal Lobectomy:* The profound changes which follow bilateral ablation of the temporal lobes in monkeys (Kluver and Bucy's (12) "taming reaction") are well known. Hill *et al.* (10) have previously reported specific changes in personality seen in some of the patients in our present series—after unilateral temporal lobectomy. These include "changes in intellectual functions, a reduction in aggressiveness, a turning in of aggressiveness with a tendency to depressive mood, changes in sexuality" (usually in the direction of more normal sexuality), "and an increased warmth in social relationships". The "turning in" of psychological attention after temporal lobectomy is of particular interest. There is often a change in the direction of psychiatric symptomatology. Outwardly expressed—"projected" symptoms tend to be replaced by inwardly directed—"introjected" symptoms. Aggressivity and paranoid projection may give way to depression and hypochondriacal anxiety. The evolution of new psychiatric symptoms after operation is not necessarily indicative of deterioration but may represent this effect of temporal lobectomy on the pattern of the patient's psychological illness. Generally the neurotic patients retained neurotic symptoms, often in changed form, for some time before they finally improved or responded to treatment. The aggressive patients, on the other hand, usually lost their aggressive symptoms with seizure control but remained liable to episodic severe depressive reactions, which fortunately responded well to early treatment.

Whilst it is generally accepted that unilateral temporal lobectomy has no effect on intellectual capacity as judged by I.Q. tests, certain specific deficits of cognitive function occur depending on which temporal lobe is removed. Meyer and Yates (14) have shown that a specific auditory learning deficit almost invariably follows dominant (but not non-dominant) temporal lobectomy. Such subjects can learn and retain normally material which they see or touch but not material which they hear. Verbal instructions are rapidly forgotten unless the patient at once writes them down and reads what he has written. These patients, however, usually adapt themselves to this difficulty and soon acquire techniques of retaining important information without relying on auditory learning. Only in the case of students (this is so far theoretical) or patients in certain occupations (e.g. telephonists) does it remain any disability. Milner (15) has demonstrated specific difficulty in the comprehension of pictorially presented concepts with non-dominant temporal lobe lesions and after recessive lobectomy but this too does not seem to lead to any noticeable post-operative deficit.

In our experience the physiological sequelae to unilateral lobectomy rarely constitute any practical disability in patients of stable personality. Neurotic patients on the other hand may complain of a variety of vague symptoms—mental fatigue, poor memory, lack of concentration, etc. Such deficits are not substantiated by psychological tests. The symptoms are usually psychoneurotic in origin and respond to psychological treatment. We have not encountered the severe recent memory defect reported by Penfield and Milner (16) after unilateral temporal lobectomy in two cases where there was also evidence of severe pathology in the contralateral temporal lobe.

Post-operative Psychiatric Management

Patients usually remained in hospital for four weeks or more after operation. This ensured surgical convalescence and allowed for a more adequate assessment of the patient's post-operative psychological status. Whilst many of our patients developed some degree of mild depression and hypochondriacal anxiety, acute symptoms during this period were relatively rare. Transient confusional states with mental symptoms or exacerbations of longstanding neurotic symptoms were occasionally seen but the most important problem was the recognition and early treatment of depressive reactions.

Acute Depressive Reactions: In our experience patients who have undergone anterior temporal lobectomy remain liable to acute depressive episodes for a considerable period (2 years or more) after operation. This depression may reach psychotic intensity, with motor retardation, agitation, paranoid or hypochondriacal delusions, etc., and may closely resemble the "acute endogenous depression" of the psychiatric ward. Fortunately such states usually responded well to electro-convulsive therapy—and we have not encountered the development of a permanent psychosis following lobectomy in a patient of previously non-psychotic personality. This liability was especially marked in patients who had shown aggressivity ("the turning-in of aggression with depressive mood") but was not confined to such cases and 2 of the seven patients whose personality had been assessed as normal before operation developed acute depressions between six and twelve months after operation. Both recovered satisfactorily with E.C.T. The occurrence of very brief episodic depression or of alternating milder depression with paranoid irritability during surgical convalescence may forewarn of later severe episodes—but occasionally delayed acute depressive states occur unexpectedly. The importance of the early recognition and evaluation of post-lobectomy depressions cannot be overstressed not only because of their potential severity (one patient in the series committed suicide) but also because response to early treatment is usually excellent.

Neurotic States: Nearly half the patients in the series had shown neurotic features to some extent or another in addition to epilepsy and many of these cases developed temporary exacerbation of these psychiatric symptoms in the months following operation. Eventual response to further treatment was, however, the rule.

The tendency after temporal lobectomy for the development of introspective neurotic symptoms (depression of affect, hypochondriacal preoccupation, depersonalization symptoms, etc.) sometimes led to a mild atypical depressive picture resembling neurotic "reactive depression". It was important to differentiate this from the "acute post-lobectomy depression" referred to above, since such states did not do well with E.C.T. and prolonged hospital admission was best avoided. No sharp phenomenological distinction (except perhaps severity or the occurrence of psychotic symptoms) could be made and it was occasionally necessary to re-admit a patient briefly to assess the significance of the depression.

Recurrent episodes of acute anxiety symptoms were also fairly common. They were rarely severe enough to need re-admission and usually responded to out-patient treatment although occasionally persisting for a year or two after operation. Patients of "longstanding hysterical personality" on the other hand, rarely did well from a psychiatric standpoint. Hysterical patterns of behaviour persisted and the patients (often their family also) blamed any new crisis on the results of operation. Such patients are crippled by their personality rather than by their epilepsy and lobectomy is probably best avoided. The occurrence of hysterical conversion symptoms in the early convalescent stage or later in patients of more stable basic personality was occasionally seen and was of less serious significance therapeutically. Two of our patients (both married women in their thirties) developed unexpectedly severe hysterical states about a year after operation (the one hysterical fits, the other bizarre fugue-like behaviour). Although both had been regarded as of only marginal neurotic personality before operation, there was evidence of hysterical traits in their pre-epileptic history and in both instances transient mild hysterical symptoms had been noted during surgical convalescence. Fortunately in both patients the symptoms responded to treatment, and we have not seen the development of persistent hysterical states after lobectomy in the absence of a clear hysterical personality pattern.

Generally, exacerbations of neurotic symptoms in the post-operative period were related to personal stress situations (marital conflict, dependency problems, etc.) and were best treated by out-patient psychotherapy. Neurotic patients were only re-admitted to hospital to achieve some specific therapeutic aim or on occasions to assess the significance of a depressed affect.

TABLE V

Hospital Treatment Following Operation

Pre-operative Personality	No.	Post-operative Hospital Treatment		
		Required Re-admission	E.C.T. Therapy	Remaining in Hospital
Aggressive	20	7	1	2
Psychotic	7	3	2	0
Neurotic	14	8	4	1
Deteriorated	3	1	1	0
Defective	4	2	0	2
Marginal normal ..	24	6	3	0
All cases	72	27	11	5

Table V details the 27 patients (37·5 per cent. of the total) who required further in-patient psychiatric treatment following temporal lobectomy. Eleven patients (15 per cent.) required electroconvulsive treatment for acute post-lobectomy depression. The response to early treatment was very satisfactory and at the end of the period of survey only 5 patients (of whom 2 were of defective intelligence) remained in hospital.

Supportive Treatment: In our view it is extremely important to see patients regularly and as frequently as possible on an out-patient basis for a considerable period after operation. Only in this way is it possible to recognize the psychiatric as well as the neurological problems of convalescence, and to deal with these as they arise. This is particularly important in the case of "post-lobectomy depression" but applies also to other psychiatric conditions which may be rapidly amenable to early treatment but may provide much greater therapeutic problems later. A combined "neuropsychiatric" supportive regime also avoids the need for attendance at different clinics with the possibility of unwittingly conflicting medical advice or management. Patients who lived at a distance from the Unit, were, of necessity, seen less frequently; nevertheless regular out-patient visits were insisted on. Where possible also patients were visited in their homes, and there is little doubt that such visits often allowed a much more adequate assessment of the total situation than could be obtained from clinic visits.

A large proportion of patients were offered regular out-patient supportive psychotherapy and in some instances this was continued for two years or more after operation. The aim was to help the patient to gain some understanding of his neurotic problems and of his characteristic patterns of dealing with these, as well as to deal with individual symptoms as they arose in relation to the patient's total life situation. For example, many patients are able to deal with the transient relative impotence which often follows temporal lobectomy without undue anxiety. One such patient developed progressively severe impotence and acute anxiety attacks which occurred at work and at home in the evenings. He was an essentially immature dependent individual whose relationship with his somewhat dominant wife had never been very satisfactory. In psychotherapy he was able to realize that his anxiety attacks always occurred in situations where his masculine role seemed somewhat threatened. With this his anxiety and impotence cleared up and his marital relationship slowly improved. Viewed in this light many of the symptoms which may seem to emerge after lobectomy are seen to be a continuation of the patient's neurotic difficulties into the post-operative situation. Psychological treatment may be particularly effective in the post-operative period when the physiological and psychological changes resulting from surgery are manifest.

Rehabilitation Therapy: Another aspect of post-operative management may be termed "rehabilitation therapy". Long-established patterns of social behaviour are not easily relinquished. The epileptic patient is often cast into the role of unemployable invalid—and thus regarded by his family, neighbours and even by the social agencies with which he has previously come into contact. Some patients will need considerable social help and support in picking up the threads of life once again.

Much can be achieved by discussing the problems with the patient's family, his medical practitioner, the disablement resettlement officer of his local labour exchange, etc., and formulating a rehabilitation plan whilst he is still in hospital.

Almost half the working population of our series were unemployed before operation and many had little occupational experience to offer a future employer. The provisions of the Industrial Rehabilitation Services of the Ministry of Labour and National Service may be eminently suited to the long unemployed epileptic whose seizures are controlled providing that any residual personality disorder is not too severe. These include resident or non-resident courses at Industrial Rehabilitation Units which offer aptitude testing and vocational guidance, followed by paid employment in sheltered conditions: as well as more prolonged vocational training schemes in a variety of skilled trades for suitable candidates. Such patients were usually seen in conference with the Disablement Resettlement Officer before their discharge and arrangements made to commence about 3 months after operation, by which time full surgical convalescence was usually complete. Generally we found it wiser for patients not to be placed on the Disablement Register if they could obtain employment otherwise, as they often felt that this carried on the stigma of epilepsy. Apart from the patients of defective intelligence only 4 were persistently unemployed (3 others were still in hospital) at the end of the follow-up period although a number of these employed were still having occasional epileptic seizures. This successful result is perhaps also a measure of the personality improvement which follows temporal lobectomy since our experience accords with that of other authors that personality disorder is a greater bar to employment than epileptic fits alone.

The use of other rehabilitation measures—social care work with the patient's family, the organization of social agency aid, etc., will depend upon the individual patient's need. Two cases may be cited briefly to illustrate the type of problems we have met.

A 26-year old girl (Case STR), previously an intractable epileptic, has suffered only very occasional nocturnal seizures since her operation 5 years ago. She has continued to live at home in poor economic circumstances with her aged and rather over-protective parents. She has no social life and few friends although her personality is otherwise normal. She is still regarded in the small town where she lives as a girl who "has fits", and all are so resigned to the fact that she will never obtain employment or get married, etc., that no effort has ever been made to alter the situation. Any attempt to help is acknowledged with gratitude, but met with passive resistance. She is still unemployed.

A 17-year old girl (Case REN) had a history of epileptic seizures dating from infancy and of an aggressive personality disorder from late childhood. At 13 years she underwent temporal lobectomy and has been completely fit-free since. After operation she attended a boarding school and satisfactory reports were obtained of her improving personality until the family moved to a seaside town some distance from London and she left school. From this time her parents complained of increasingly severe aggressive conduct on her part. This had become so bad that on two occasions they had contacted the duly authorized officer and asked for her to be admitted to a mental hospital. It was felt that an adequate assessment of the situation could not be made from out-patient visits so the author visited the family at home and discussed the problem with the patient's general practitioner. It was clear that the family was an unstable one. Two younger siblings had overt behaviour disorders and both parents themselves showed some degree of psychiatric disturbance. The situation was then discussed at a conference with the children's officer, D.R.O. and the D.A.O. and arrangements made for her to go to a residential secretarial training college. The case was also discussed with the physician of a nearby psychiatric hospital, but admission proved to be unnecessary. After 9 months at the college she is now living at home, is much improved and is holding down a job successfully. She no longer feels depressed and unwanted, and the improvement is due in no small measure to the support and co-operation of the various individuals concerned in her care.

The value of a conference attended by the various medical and non-medical individuals concerned in a patient's welfare, at which the problems are discussed in detail in their differing aspects is often considerable in producing personal interest and co-operation in the patient's rehabilitation.

Discussion

Of the 68 patients with normal intelligence submitted to temporal lobectomy for psychomotor epilepsy 65 per cent. showed marked and 25 per cent. less severe personality disorder in addition to their fits. Recovery or considerable improvement in psychiatric status followed operation in 41 (57 per cent.) of those cases with personality abnormality whilst only 8 (13 per cent.) were unchanged or worse.

These findings are in close agreement with those reported by Alajouanine, Nehlil and Houdart (1) and we would concur with these authors that the best results are seen in patients with severe aggressive character disorders but that the outcome is much more variable in patients with minor psychiatric troubles. Nevertheless substantial improvement has occurred in a good proportion of patients with certain neurotic disorders.

We find it difficult, however, to reconcile our experiences with the results published by Simmel and Counts (20) who reported personality deterioration in 16 of 40 cases studied after lobectomy. They assessed 10 cases as having been "psychotic" before operation (21 others were assessed as "marginal" and 8 "O.K."), but found 14 "psychotic", 19 marginal, and 7 good on follow-up survey. Using the term psychotic in the sense in which it is currently used in psychiatry to describe certain acute mental states (characterized by schizophrenia and manic-depressive psychosis) in which particular symptom complexes implying a "break with reality" occur and to differentiate such states from psychoneurotic and psychopathic conditions, only 7 (10 per cent.) of our series provided a history of psychotic illness. All but one of our 7 cases had suffered from episodic psychotic states with periods of remission or at least improvement. All had been judged before operation to have a poor psychiatric prognosis with the expectation of increasingly severe recurrent or permanent mental illness. Most were operated on during remission or partial remission of the acute symptoms and the results have been very satisfactory (4 recovered or substantially improved, 1 improved, 1 unchanged, and 1 died during follow up).

We have not seen the emergence of a persistent psychosis after operation where it has not been present before.

Psychotic symptoms—depressive delusions, etc., may occur in the acute post-lobectomy depressive reactions which are to be expected in between 10 and 20 per cent. of patients submitted to operation, but these states are temporary and usually respond rapidly to electroconvulsive or other psychiatric treatment.

The treatment of the psychological sequelae to an operation designed to control epilepsy by means of electrically induced convulsions is not as paradoxical as it may at first seem. The treatment is in no way a substitution therapy —the substitution of induced seizures for spontaneous fits. The physiological accompaniments of E.C.T. are probably very different from the physiological sequences in epileptic seizures. It is an empirical treatment for the acute post-lobectomy depressive reaction and the response to E.C.T. resembles that seen in the acute endogenous depressions of later life.

Our data suggests that the relationship between the epileptic process and the personality disorder is a complex one. Generally there was a direct correlation between the severity of the pathological process in the mesial temporal structures and the severity of the psychiatric disturbance. The form of the personality disorder on the other hand did not appear to bear any direct relation to the pathological findings, and here it would seem that such factors as constitutional variation, environmental influence and the state of personality maturation at the onset of the overt epileptic disturbance operate.

Many of the patients who developed neurotic disorders provided evidence of a family history of neurosis or of a disturbed family environment. Aggressive conduct disorders were proportionately more frequent in patients from lower social class homes (i.e. social classes 4 or 5 of Registrar General's Classifications).

Another statistically significant factor was the age of onset of overt epileptic fits. All but one of the patients with severe aggressive conduct disorder had developed seizures before the age of 13 years. This group also had a significantly lower I.Q. than the remainder. The lower intelligence level can only be accounted for in part by the frequency of Ammon's horn sclerosis in these cases. It is probably also due to the educational disruption occasioned by fits and drug therapy during the school years as well as to a poorer genetic endowment as evidenced by the lower occupational records of the parents. Most of the patients who developed neurotic disorders on the other hand started to have fits during adolescence whilst patients who did not develop epilepsy until adult life showed much milder psychiatric disturbance. It would accord with the general experiences of child psychiatry to suggest that personality disturbance commencing before puberty is more likely to be manifest in the spheres of emotional control and conduct, especially in individuals of lower basic intelligence, whilst with increasing age and I.Q. neurotic personality formation is more frequent. Once adult life is reached, however, the personality structure is less vulnerable to the onset of epilepsy unless some overt or latent defect of adjustment exists.

Whilst the primary aim of temporal lobectomy is the control of otherwise intractable epileptic seizures, considerable psychiatric improvement may follow operation provided that the criteria for the selection of cases are strictly adhered to and that psychiatric treatment is continued where necessary for a considerable period after operation.

ACKNOWLEDGMENTS

The author wishes to express his gratitude to Mr. Murray A. Falconer and to Dr. Denis Hill for permission to publish details of this study of cases under their care, and also for their kindness, help and supervision during its completion. Professor A. Meyer, and Dr. J. B. Cavanagh kindly gave the pathological details.

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THE "BRAIN FAG" SYNDROME IN NIGERIAN STUDENTS

By

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I. INTRODUCTION

THERE has recently been a good deal of concern expressed in the Press, both of Nigeria and Ghana, over the high incidence of psychiatric disturbance among West African students in the United Kingdom. Whether the incidence of such disturbances is in fact greater among Africans than among other foreign students in the British Isles is not known; nor has it been determined whether the African student abroad is more prone to illness than his counterpart studying at home. Relevant to the latter question, it is clear that a high proportion of the cases seen in the psychiatric clinics both at Aro Hospital, Abeokuta and at the University College Hospital, Ibadan, are students, teachers and other "brain workers" who have never left Nigeria.

Although no figures are available, there seems to be a distinctly higher proportion of students attending the psychiatric clinic in Nigeria as compared with Canada.* In Canada there is a much greater percentage of housewives, labourers and factory workers and a relatively small teacher and student group. This difference in proportion could of course be explained in other ways than as being a difference in actual incidence in the two countries. For example, it is no doubt important to note that the housewife or labourer in Nigeria would attend native treatment centres whereas the more sophisticated group of students and teachers tend to seek out the "Europeanized" psychiatric clinics.

It is proposed in this paper to delineate and discuss what appears to be a distinct psychiatric syndrome occurring in Nigerian students and other "brain workers". It is very common. As one medical officer remarked to me, "If a young man comes in with glasses and European dress, you may be sure that he will complain of burning in the head and inability to read." For the present study many cases were seen before it was realized that the condition was a distinct syndrome. Ten cases were selected for more intensive investigation.

II. THE "BRAIN FAG" SYNDROME

The distinctive symptoms of the syndrome are intellectual impairment, sensory impairment (chiefly visual), and somatic complaints most commonly of pain or burning in the head and neck. In addition there are a variety of other complaints that often militate against the student's ability to study. The patients have an unhappy, tense facial expression and a characteristic gesture is frequently noted—that of passing the hand over the surface of the scalp or rubbing the vertex of the skull, especially when discussing a question that requires concentration.

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* The author has had five years' experience in various psychiatric clinics and mental hospitals in the vicinity of London, Ontario, a small university city in Eastern Canada.

The syndrome is commonly observed in adult unmarried Nigerian males between the ages of 15 and 30, who are students at secondary school or university or teachers or government clerks who are studying in their spare time to raise their educational level. It has been most commonly seen among the Yoruba,* no doubt because the centres of investigation for the present study are in the heart of Yoruba country. However, it has also been observed in the Ibos of the Eastern region and among the Edos of the Benin area as well as in other smaller tribal groups. It has not been observed among the Hausa of the Northern region, possibly because of some basic difference in personality structure, but more probably because Hausa people are not commonly found in the role of teacher or student in the area of investigation.

Intellectual Impairment

Unlike the symptoms emphasized by the Canadian and European neurotic (i.e. anxiety, depression, insomnia, palpitation, obsessive thinking, etc.), this group of patients stress their difficulty in mentation. They complain that they are no longer able to read, or grasp what they are reading, or cannot recall what they have just read. In some cases they cannot remember anything that they have ever studied. They are unable to concentrate and a lecture seems just "words without significance".

"When I read I don't assimilate anything, and when they teach me my mind will not take it in. I forget the word that I am supposed to be looking up in the dictionary as I am leafing the pages. If I pick up a book it seems that a boy of five is looking at it, the letters don't mean anything. I have forgotten all that I learned; it is as if I had no past. When someone talks to me, it doesn't go to my brain. When I talk it doesn't seem to come from my brain at all, but just from my mouth." "I will sit down to read but I am just helpless, my mind isn't there. I cannot write. I have given up writing letters and send telegrams instead. I will read several pages and realize I can't remember a thing I have read."

Sensory Disturbances

Patients complain chiefly of visual disturbances and sometimes of auditory difficulties. The patient knows that he sees and hears well, but feels that there is some alteration in these faculties which he finds difficult to describe. He often describes these changes in a metaphor. They occur chiefly when the patient is dealing with the subjects of his study or with other material requiring increased concentration.

"I can't seem to see the page; if I look at it, it seems as if I'm blinded by a light." "Whenever I want to do a hard job, something passes through the back of my head and I have the feeling of dazzling in my eyes and I am confused." "When I look at writing there is a strain across my eyes and my eyes are dim." "Something seems to come down over my eyes like a hood when I am talking or reading, though actually I see very well—it's just the way it seems."

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* For further details about the people and social conditions of this area the reader is referred to Lambo (4).

Somatic Complaints

Concomitant with these intellectual and sensory difficulties and often preceding them in the course of the development of the disease, there is almost always complaint of disagreeable somatic sensations, chiefly involving the head and neck. This may be described as pain in the back of the neck and over the occiput, frontal headache, burning sensations over the scalp ("as if pepper had been rubbed into it"), a burning sensation in the centre of the head, "like a piece of red hot iron", a feeling of waves passing over the scalp, a feeling of vacancy in the head, etc. These symptoms may come on when the patient attempts intellectual activity or may be present continually with exacerbations when study is attempted.

As with most functional illnesses, in addition to these head symptoms there are consistent complaints of "general weakness of the body" and easy fatigability. Sometimes there is a special weakness or "shakiness" of the right arm which impairs writing.

Insomnia is not as common as one might expect and in some cases the patient complains that he sleeps too much. There is often an exaggerated difficulty in getting out of bed in the morning to go to school or to work. One of the patients described falling asleep in lectures but later as the process advanced he began having difficulty in sleeping at all.

Dizziness and "loss of balance" is a common complaint. In one case this symptom dominated the picture and the patient was afraid to ride his bicycle for fear of falling. This symptom prevented him from going to school.

Excessive perspiration, "foul breath" and stomach complaints occurred less frequently. Anorexia was uncommon in this series.

As regards the sexual life of these patients, the majority are unmarried and many of them say they have given up dealings with women to allow themselves to give their full energies to their studies. Impotence was complained of in several cases. In one case, the symptoms began during masturbation. Another patient reported that he experienced orgasm during the writing of an examination, "During the first examination paper, I passed out semen while I was writing. I wasn't able to write at all; I was oblivious of my surroundings."

Alterations in Affect

Alterations in affect are not generally stressed. If questioned specifically, some describe a feeling of depression, which is most marked early in the morning. In two cases however, depression did seem to be a major feature. Both cases were students who had suffered the illness for several months and, while attempting to study for examinations, became very depressed with suicidal fantasies so that their school principals became alarmed and sent them to the clinic. Both felt that they had become depressed as a result of being unable to study rather than that they had been unable to study as the result of their depression.

Precipitating Factors, Course and Prognosis

In most cases no definite precipitating factor was known to the patient. Most often the symptoms commenced during periods of intensive reading and study prior to examinations or sometimes just following periods of intensive study. The patients themselves generally attribute their illness to fatigue of the brain due to excessive "brain work". It is for this reason that the designation "Brain Fag" syndrome has been used. The expression seems to be used by

Nigerians generally to describe any psychiatric disturbance occurring in "brain workers".

In the ten cases studied more intensively several were able to suggest precipitating factors in addition to "too much study". In two cases the symptoms commenced following failure in an examination and a third noted a marked exacerbation in his symptoms after a failure. One patient began to suffer symptoms immediately after successful surgical removal of his duodenal ulcer; in this latter case there seemed to be a substitution of symptoms. Two other patients noted the onset of their symptoms following an episode of "fever"—presumably malaria.

The onset is usually gradual, the somatic symptoms in the head commencing before the intellectual impairment. The patient notices the burning in the head while reading heavy material but is able to read newspapers and other light material without difficulty. Later, symptoms occur with intellectual activity of any kind, and finally the symptoms may be present continually and the patient isolates himself from all serious intellectual activity.

Because of the short period of observátion covered in the present study (one year), no definite statement can be made as to prognosis. However, mild, early cases seem to respond rapidly to treatment. Some severe cases of long standing persist in spite of intensive treatment and force the patient to give up further study.

III. Case Histories

(I) A.B. is a 28-year-old Yoruba male, unmarried, who is teaching Latin and English at Grammar School, and is taking an Honours Degree in Classics by extension from the University of London.

The father was an illiterate trader and farmer who had two wives. According to the patient, the father was a harsh man who used to beat him twice a day. He was said to be under the domination of his second wife, the patient being the son of the first wife. He wanted the patient to be a trader and discouraged him from taking any higher education.

The mother was also illiterate and a staunch Roman Catholic. After ten years of childlessness, she was overjoyed at the birth of the patient; she spoiled and petted him—and breast-fed him until at least the age of four. He can remember running home from school and "worrying his mother to give him the breast". When he was punished or thwarted, he had "fainting attacks", involuntary at first, but later he learned to "do it on purpose" to get his own way.

At school he was bright and led his class throughout. He began teaching school in 1949, taking his B.A. degree by extension at the same time. He first began to notice symptoms after writing the B.A. examination in 1953. He felt weak and could not concentrate for about two weeks. Symptoms recurred in 1956 when he was studying for the Classics examinations. He began to have sharp pains in the head and could not grasp what he was reading. He slept more than usual, and had difficulty in forcing himself to go to school in the morning. When writing the examinations, he felt that he knew the answers, but was unable to recall them; his mind was blank. His right hand was weak and shook so that he couldn't write. Because of these symptoms, he was forced to postpone writing the examinations for two years. His symptoms improved greatly with Largactil and reassurance.

(II) S.A. is a 21-year-old single Yoruba male who is attending Teacher Training College.

The father was an illiterate farmer with two wives. The mother was a cloth seller and a "very quick tempered woman". The patient is the youngest of three male children. The two eldest are successful farmers. Both mother and father were anxious for the patient to obtain a good education. The mother and one of the brothers paid his school fees.

The patient was a healthy child and was breast-fed until about the age of three. He feels that he had a happy childhood, and except for nail biting, he remembers no "nervous" symptoms. At school he performed well, never standing below 4th out of 30 students. He taught school for three years before entering the college where his symptoms commenced.

He started his course in January, 1958, and after three months began to feel weak and used to fall asleep during lectures. Later he noted that he was not assimilating what he read or what he was taught. His scalp became tender and when he talked he had pains in his legs. Subsequently he became depressed and felt that since he could not learn any more, he was useless. He sometimes contemplated suicide.

He was given a course of E.C.T. with tranquillizing drugs, his symptoms cleared considerably, but he has not yet returned to school.

(III) S.L. is a 29-year-old, unmarried Yoruba male, who is a Baptist student minister and studying for the West African School Leaving Certificate.

The father was a farmer and trader, sufficiently literate to be able to read "a little of the Bible". He is described as a man who "acted on impulse" and was easily irritated. He had three wives and twelve children.

The mother of the patient died of "stomach trouble" when the patient was three months old, and he was brought up by his grandmother.

As a child, the patient was sickly and cried a lot. He was not breast fed at all—except for perhaps the first month or two. He feels that he was unhappy as a child "for want of a proper mother". He suffered frequent nightmares and developed stomach trouble when quite young. A duodenal ulcer was diagnosed in 1948 and he had two operations. Following the second operation in 1955 his stomach complaints disappeared, but almost immediately he developed "head trouble". Whereas before the operation he could read with a thorough comprehension, afterwards, he had difficulty in grasping and recalling what he read. Because of this, he failed an examination and then his head symptoms became noticeably worse. He developed a dull aching pain over the vertex of his skull, and a tingling in the scalp. He was unable to concentrate on what people said to him, and he complained of excessive perspiration.

His symptoms improved considerably with Largactil and phenobarbital, and he has been able to resume his studies effectively.

This patient is very dependent and has a strong need to please. He feels that he has a special ability to secure favourable answers to prayer and spends many hours in praying. He also has the "gift of tongues" and at times has the ability to prophesy in a strange language. He does not understand this language, but feels that he is expressing what is in his mind. He daydreams a lot . . . most often about going to America and making $20,000 and then returning to help his people and buy them all automobiles.

At school, before his illness, he was an average student, and his course is being financed by an American sponsor.

(IV) G.B., a 28-year old Edo male, is a mechanic, and was taking a motor mechanics technical course by extension, until his symptoms appeared.

His father was literate, and worked as a storekeeper for the Public Works Department. He had two wives. The patient has four older sisters.

He feels that he was "spoiled" as a child because his mother was very pleased to have a son. He was breast fed until the age of four, which was longer than any of the other children. He commented "My mother never flogged me, but let me do whatever I wanted until I was six years old, when I went to live with a relative who taught me discipline."

He went through elementary school and was an average student. After completing his schooling he became an apprentice motor mechanic. He studied to be an "automobile engineer" in his spare time, and it was necessary for him to read a good deal. In June, 1957, he began to suffer head pains after reading for an hour or two. The symptoms gradually grew worse until he found that if he tried to look at a page of print, he would have pain across the eyes, and his vision would become dim. The same symptoms appeared if he had a difficult mechanical job to do. He began to be very forgetful and confused, so that he often forgot where he left his tools, and how to use them. His symptoms improved somewhat on Largactil, but he did not resume his studies.

IV. Special Features in the Histories

In attempting to clarify possible aetiological factors, certain areas in the case histories received special attention. The following are summaries of the results.

Parental Literacy

Nigeria is a country undergoing rapid social and technological change. It was thought that the student might have difficulty in using his intellectual faculties in the highly abstract and disciplined way required by higher education, without a social or family tradition. It was found that in one of the ten cases, both the father and mother were literate; in three others, the father alone was literate and in the remainder the patient was the first generation literate. In none of the cases were the grandparents literate. Although the numbers are too small to allow any definite conclusions to be drawn, it would seem that parental literacy does not provide any marked protection from the illness.

Breast Feeding

By European standards, the Nigerian mother breast feeds her child for a prolonged period. Matthews (7) studying women who attended the post-natal clinic at Adeoyo Hospital, Ibadan, noted that not one mother had voluntarily weaned her baby before the tenth month, and that of some 540 patients attending the clinic within 15 months of parturition, only 4 had totally weaned their babies.

It would appear that breast feeding often continues to the age of two or three years, or possibly longer. The breast is for the most part given "on demand" whenever the child cries. There is very close physical contact between mother and child during this period. The mother may commonly be seen walking along the road to market in the morning with a great load of calabashes poised on her head and the baby tied to her back with its head poked under her left arm sucking contentedly at the breast. The child is usually weaned at the time of a subsequent pregnancy, which are usually spaced three years apart. Disagreeable tasting substances placed on the nipples are sometimes used to promote weaning. Many patients are able to recall breast feeding. In the present study five patients were not sure how long they had been breast fed, three had been fed until the age of three and one until the age of four. In the remaining case the mother had died when the patient was three months old and the patient had never been breast fed. It was this patient that subsequently developed a duodenal ulcer (Case 3).

Polygamous Family

The Yoruba is traditionally polygamous, the number of wives depending upon the extent of his fortune. The father is the head of the home, followed by his eldest son in matters of authority. The wives have a hierarchy of authority, the first wife often being exempt from household duties and the most junior being responsible for the most menial tasks. The relationship between husband and wife appears to be distant—almost formal—and the relationships between mother and child proportionately more intense. There is a quite open preference expressed for a male child. Relationships between the wives are often strained, especially if one of the women is childless or if her children die young. Such occurrences rouse suspicion of witchcraft or "medicine" and tend to draw the mother and her children closer together. Mabogunje (6) gives an interesting picture of the hostility between wives, and some of their modes of handling it:

> "Among the women, the first symptom of a disagreement is a refusal to greet. In a family where women see so much of one another all the time, the effect of this grudging can be immediate on the person so grudged. If the person grudged is of a more peaceful disposition, or, if she desires a stronger case when the quarrel bursts out into more boisterous forms, she might start by trying to ascertain the cause of this behaviour. She might even succeed to nip the quarrel in the bud. If however, she is the haughty type, she counters the refusal to greet by a fight with her eyes. She looks at the other woman in a way to attract the latter's attention. When their eyes meet, she turns her head away slowly and with her eyes gradually shutting as she does so. This way of looking at the other woman is contemptive in its meaning and is usually very provocative of a more noisy outburst. Sometimes the fight with the eyes takes the form of looking the other woman from the head to the foot, and hissing loudly in the process.
>
> More interesting than any of the above is the quarrel when it takes the form of singing at the other woman. The songs are spontaneously composed. It is not the music that matters as the words, which are made up from proverbs, leave no one in doubt as to whom they refer to. This form of the quarrel often takes place where other women are sure to hear the song, for instance at the laundry place. It is extremely provocative, and usually, if the other woman cannot match such ingenious composition, she loses her self-control and may resort to violence. If she doesn't, she might resort to the more prosaic form of abuse—in truth, making a verbal caricature of her opponent."

In the present study, nine out of ten patients derived from polygamous homes. It will be clear that the atmosphere of the polygamous family and its effect upon the psychology of the children requires much further investigation.

Intelligence

No formal intelligence tests were given. Some rough estimate of the patient's intellectual abilities was made during interviews and from the student's appraisal of himself. In some cases it was possible to interview the patient's teacher. It was felt that the syndrome was not related to intelligence. Two of the patients were on scholarships and three others were "above average", four of the remainder were considered to be "average", and one "dull".

Social Aspects and Motivation

Education is at a premium in Nigeria today. It is the road to wealth and prestige, which, with fecundity, appear to be the major values in the culture. Education is often a family affair in that one of the brighter children may be supported financially by some member of the family or group of members—brothers, cousins, uncles, etc. The educated member, in his turn, is expected to be responsible for other family members should the need arise. Because of this "family affair" aspect of education, the student is very much the centre of attention and the burden of family reputation and prestige often rests upon his shoulders. His success or failure, then, looms large, and much more is at stake than for the European or American student. How important a part these factors play in the genesis of the syndrome is difficult to appraise. The patients themselves tend to minimize these factors. It was clear, however, that success in their education represented a very major need for all of these patients and two of them declared that they would "rather die" than give up their schooling.

V. Discussion

The present study has attempted to delineate one of the most common psychoneurotic syndromes to appear at the psychiatric clinic in the Western Region of Nigeria. Because of the scarcity of psychiatric observers and limited facilities, previous studies in African psychiatry have dealt largely with the psychoses and particularly with the psychoses in which anti-social behaviour required that the patient be confined in a "lunatic asylum" or mental hospital. With the recent opening of the Psychiatric Out-Patient Clinics at Ibadan and Abeokuta, it has been possible to observe some of the psychoneurotic patterns as they occur in these areas.

The most common psychoneurotic pattern is clearly that of somatic complaint. This takes the form of pain or burning in various parts of the body, the sensation of worms moving about the body, chest tightness, etc., accompanied usually by weakness and insomnia. Hysterical symptoms are also common, not so much among the illiterates as among those with a moderate educational level such as elementary school teachers, and junior government employees. Hysterical paralyses, astasia-abasia, breathing disorders, tics, deafness, aphonia, tubular vision, strange posturings, and other patterns have been observed. The "brain-fag" syndrome seems to partake of both hysterical elements (in the disorders of special senses and of mentation) and of the somaticization of conflict. It appears to be more common among the better educated components of the community or those attempting to attain higher education.

Some of the commoner symptoms observed in Canada and Europe are rare in Nigeria. Depression of any depth is seldom seen and the threat of self-castigation is very rare. Suicide is unusual and the "appeal" type of half-hearted suicide attempt has not been observed. Alcohol and drug addiction and sexual perversions are rare, or at least do not find their way to the clinic. Obsessive-compulsive neuroses or symptoms and phobic reactions are equally rare. When these uncommon types of symptoms do appear they occur in the more highly Europeanized elements of the community. The present author's experience tends to confirm Lambo's (3) observation that the more westernized the individual becomes, the more the psychiatric pattern he develops tends to conform with the patterns found in Europe and America. What exactly is involved in being "westernized" in this sense is not yet evident. It does seem to be clear that genetic elements are not of major importance in determining these patterns. Is it necessary however for the individual to be reared as a western child from infancy (with very early weaning, rigid toilet training and highly personal discipline), or could an individual develop an obsessional neurosis or alcoholism simply through teaching him a European language and immersing him in a European milieu after being raised in a typically Yoruba fashion until the age of four or five? These are interesting problems for further research.

There is one major difficulty in attempting to make any but speculative comments upon the psychodynamics of Nigerian neuroses. This lies in the Nigerian's apparent lack of need to engage in the elaborate introspections and soul searchings in the way the European does. Because of this lack of interest in expressing himself concerning his own subjective experience, it has been difficult for the author to employ the non-directive interview technique, even with the highly educated patient where the language barrier is not a problem. Even when direct leading questions are finally resorted to, it has been impossible to encourage the patient to make any but the most cursory remarks about his relationships with his parents or other people. For example if a patient is asked what kind of a man his father is he will in a word or two describe his physical appearance and may say what his occupation is, but will scarcely seem to understand when pressed about his father's temperament or emotional characteristics, or his father's feelings toward him. Further it has only been possible on rare occasions for the patient to establish any clear-cut causal connection between his symptoms and his emotional life.

Several possible reasons may be suggested for this failure of the non-directive and free association techniques with the Nigerian. Firstly, one might mention the intense oral orientation of the Nigerian at his present level of development due presumably to his prolonged period of breast feeding and the long period of continued "uterine" existence on his mother's back. These factors seem to lead the patient to look upon the therapist as an omnipotent figure who can magically cure his symptoms without any effort on his own part. All that should be necessary is for the patient to outline his symptoms so that the doctor can give him the appropriate injection or medicine and he will be cured. Secondly, there is no traditional concept of emotional causality for disease; at the back of the patient's mind is usually the idea that his symptoms are caused by the "bad feelings" and machinations of his enemies or of witches rather than by bad feelings in his own unconscious. Discussion of his own feelings then seem to him irrelevant. The belief in malevolent magic and witchcraft is still very potent even among many of the more westernized. An amusing anecdote might help to clarify this point. An Ibadan Grammar school teacher sent a questionnaire to her graduating class asking whether or not they planned upon returning to their home villages after graduation, and also to give their reasons. One 18-year-old student replied that he would not return because he was now the only educated person in his village and could no longer be content to live among illiterates. Moreover, he added "In my own village, I am always being worried greatly at night by the witches in the trees."

Finally it must be noted that this lack of verbal awareness is not restricted to the psychological life of the Nigerian. In considering the Yoruba language for example, just as there are no satisfactory words for depression, masturbation or homosexuality, so there are words for only three colours, viz., red, black, and white. This does not necessarily mean however that the Yoruba has no awareness or experience of these feelings or behaviours, for although he has only this limited verbal colour range he is well aware of the difference between these and other colours and employs these colours, for which he has no name, in an aesthetically pleasing way in his clothing and in his dance masks. The almost universal colour for the Yoruba woman's dress is indigo blue, yet there is no Yoruba word for this colour. It would appear that he has no need to speak of these things or to think about them verbally. Of course the reason for the author's failure with the non-directive method may well lie with himself and not with the patient, and African psychotherapists will ultimately answer the question.

Bearing these limitations in mind, some speculations about the aetiology of this disturbance should perhaps be made. It is clear that the syndrome is related to "westernization", for prior to the 19th century when significant European influence commenced, the written word and the student life, which are so intimately bound up with the syndrome, were unknown to the inhabitants of Southern Nigeria. Further, the syndrome is rarely seen in the European. It would appear then that the illness is related in some way to the fusion of European learning techniques with Nigerian personality.

In considering possible aetiological factors in the Nigerian personality, it is clear that we are in search of some widespread and fundamental traits for the syndrome is almost a stereotype, irrespective of the tribal group the patient derives from in Southern Nigeria. As has already been emphasized, moreover, it is exceedingly common and detracts significantly from the efficiency of no small number of Nigerian students.

The Nigerian character and the child rearing practices and other social influences important in its genesis have been dealt with elsewhere (Lambo and Prince (5))*, so that a summary will suffice here. The tribes of Southern Nigeria are examples of the collectivistic society as opposed to the individualistic society in Soddy's (8) terminology. The collectivistic society is characterized by the extended family and shared family responsibilities as has been outlined above in connection with the reciprocal responsibilities regarding education of one of the family members; in this type of society there is a strong sense of identity with the group and a limited sense of individual identity which probably has some relationship with the limited verbalization and self-awareness that give rise to the difficulties in insight psychotherapy already referred to; there is a marked reluctance to assume individual responsibility in circumstances of choice and a distaste for isolated endeavour; there tends to be a blind acceptance of authority and established pattern but a "paralysis" in the face of the new and a restriction of individual creativity. As additional factors in the genesis of the Nigerian personality, certain aspects emphasized by the psychoanalysts seem to be relevant. The prolonged oral satisfactions and protracted early contact with the mother give rise to strong oral components in the personality*—optimism, dependancy, a love for gift giving and receiving and a certain demanding quality. Similarly, the permissiveness as regards toilet training appears to result in the lack of the traits of the anal personality†—meticulousness, orderliness, punctuality, frugality, stubbornness and organizational ability. There is also a poorly integrated and "weak" super-ego formation. Theoretically the well-integrated and "strong" super-ego provides the individual with an internalized source of self esteem so that his self value is to a lesser extent the pawn of the opinion of the people surrounding him. When the super-ego is poorly developed the individual is dependent upon others as sources of self esteem.

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* Also compare studies on character formation in a Belgian Congo tribe by M. Th. Knapen (2).

With these character traits in mind we are perhaps in a better position to understand the difficulties of the Nigerian student involved in the Western type of student life. Western methods of education are *par excellence*, methods involving isolated endeavour, individual responsibility, orderliness and organizational ability. Western educational techniques are the product of an individualistic society where breast feeding is at a minimum, toilet training is at a maximum, where the super-ego is overbearing and every effort is made to minimize the need for external sources for self esteem. "Self reliance" is exalted. There is considerable stress placed upon verbalization and the expansion of consciousness from an early age.

It is suggested then, that the circumstances of prolonged isolated book learning and the intense individual responsibility-in-isolation inherent in the western type of "examination" system are of paramount importance in generating the painful feelings which result in this syndrome.

There is some reason to believe that the students who are more vulnerable to the disease are those who have had a more dependent and a more "bound up" relationship with their mothers. The theme of being "spoiled" by their mothers seemed to occur often in the histories. The patient was breast fed longer than his siblings; he was never "flogged"; more fine clothes were bought for him than for other family members, etc. This was not consistently the case however, and in one of the cases the patient appeared to be maternally deprived (Case 3).

The syndrome may be looked upon as an unconscious rejection of the educational system—a kind of sloughing off of the entire student life. The patient cannot read, cannot remember and cannot write. Occasionally the two elements in the conflict will emerge to some degree into consciousness and the patient will speak of two elements within himself, one that urges him on to study and attend to the lecture, the other that urges him to forget all about it and stay in bed. The syndrome represents a regression to a childlike state—"I feel helpless and it is as if a child of five were looking at the page, the letters have no meaning."

Some teachers and other observers with whom I have discussed the problem have expressed the opinion that faulty study habits are an important cause of the illness. They point out that the Nigerian spends long hours poring over his books with little relaxation. It is the author's opinion, however, that these "faulty study habits" are a further manifestation of the difficulty rather than the cause. The student forces himself to sit before his book going through the motions of study but part of his mind will not assimilate, being in revolt against this fundamentally alien mode of isolated endeavour. Some students may be seen sitting in the library before an open book, listlessly leafing the pages and "cracking" their necks to release the tension generated by this conflict between conscious aim and more or less conscious revolt.

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* For review of the oral and anal personality types see Fenichel (1).
† For review of the oral and anal personality types see Fenichel (1).

If we accept that these factors are of some significance in aetiology, are we in a position to offer any constructive advice to the Nigerian educator? Of course it is probable (whether desirable or not) that the Nigerian social structure will slowly transform itself in the direction of the more individualistic pattern, at which time we should theoretically expect the "brain fag" syndrome to disappear, and be superseded by other psychoneurotic patterns. In the meantime, it might be suggested that much more emphasis should be placed upon group learning techniques as being more in line with the requirements of the "collectivistic personality". This would of course require skilful group leaders, adept in the Socratic method of drawing knowledge to the surface and building it into consciousness through the dialogue rather than through isolated reading and didactic lectures. More emphasis should perhaps be laid upon the daily work of the student rather than allowing the final written examinations to assume such towering importance. It might even be possible to devise some group examination techniques.

Before such preventive measures could be considered however, it is important that further research be carried out to determine the actual proportion of the student population affected by anxiety of this type. If there is a sufficiently large proportion affected to warrant preventive measures, a small experimental group should be set up to determine whether group techniques of learning are of any value in allaying this type of anxiety and of reducing the incidence of this syndrome.

SUMMARY

A very common psychoneurotic syndrome occurring among the students of southern Nigeria has been outlined and discussed. The symptoms are such as to prevent the student from carrying on with his work and include various unpleasant head symptoms accompanied by inability to grasp what he reads or what he hears in a lecture, memory loss, visual difficulties, inability to concentrate, inability to write, etc.

Various possible aetiological aspects are discussed and it is felt that the syndrome is not directly related to genetic factors, intelligence, parental literacy, study habits or family responsibilities. The hypothesis is presented that the syndrome is in some way related to the imposition of European learning techniques upon the Nigerian personality. It is suggested that European learning techniques emphasize isolated endeavour, individual responsibility and orderliness—activities and traits which are foreign to the Nigerian by reason of the collectivistic society from which he derives, with its heightened "orality" and permissiveness.

It is suggested that an emphasis upon group learning and examination techniques might be of value as preventive measures as being more in accord with the needs of the collectivistic personality.

ACKNOWLEDGMENTS

I would like to thank Dr. S. Franklin, Chief Medical Advisor of the Western Region, Nigeria, for permission to use clinical material in this study.

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CLINICAL OBSERVATIONS ON THE USE OF PERPHENAZINE (FENTAZIN) IN MENTAL HOSPITAL PATIENTS

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THE value of phenothiazine derivatives in psychiatric practice is well established, but in spite of their undoubted usefulness in certain psychiatric disorders none has proved entirely acceptable. The introduction of a new derivative that is reported to be less toxic than earlier phenothiazine derivatives and highly active in small doses merits investigation and trial.

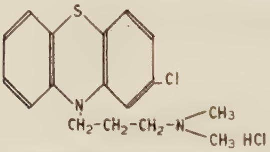
Under the name Trilafon, perphenazine has been available in America for some years and clinical reports, both on its use in psychiatry and as an anti-emetic, have been numerous. Ayd (1) gave perphenazine to 300 patients with a variety of psychiatric disturbances in whom the predominant symptom was anxiety, agitation or psychomotor excitement. He considered that it possessed some advantage over other tranquillizers in that it caused a minimum of troublesome side-effects. He stated that since perphenazine reduces anxiety without causing psychomotor retardation or other undesirable psychological reactions, it facilitates psychotherapy. Darling (4) gave perphenazine to 100 hospital patients, including 71 schizophrenics. He considered that perphenazine seemed to cause less agitation and depression than that observed with chlorpromazine, reserpine and thiopropazate.

Cahn and Lehmann (3) gave perphenazine to 84 selected patients with the following results. Of 11 acute schizophrenic patients, 5 recovered and 2 were much improved (60 per cent.) within 4 weeks. Of 8 acute manic patients 7 became asymptomatic within a month. Of 42 chronic schizophrenic patients 18 (43 per cent.) were definitely improved and 15 (36 per cent.) temporarily improved or were controlled. Nine (21 per cent.) failed to respond favourably.

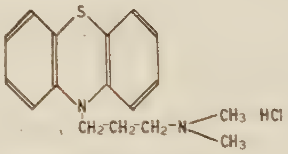
These figures include those patients who had already started to show improvement on other therapeutic agents before the administration of perphenazine and the authors felt that they could assume that perphenazine was either responsible for the improvement or was at least capable of maintaining it.

PERPHENAZINE

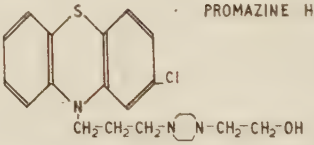
Perphenazine (available in this country under the name Fentazin and in America under the name Trilafon) is an amino derivative of chlorphenothiazine; the full chemical designation is 1-(2-hydroxyethyl)-4-[3-(2-chloro-10-phenothiazinyl)-propyl] piperazine. There is a close chemical relationship between chlorpromazine, promazine and perphenazine, as seen by their structural formulas:



CHLORPROMAZINE



PROMAZINE HYDROCHLORIDE



PERPHENAZINE

Their pharmacological effects are similar but there are considerable differences in their potency and toxicity. In experimental animals, perphenazine has been shown to be at least five times more active than chlorpromazine. Benson-Harer (2) considered that perphenazine is only one-half as toxic as chlorpromazine.

THE SCOPE OF THE TRIAL

When the use of perphenazine was started in this hospital, a true clinical trial was not envisaged. It was first used in a relatively small number of patients, to obtain a general assessment of its properties. Group controls were not used and no effort was made to give the drug to any particular type of case.

When it became apparent that some patients were responding to perphenazine who had hitherto been completely unresponsive or only slightly responsive to other forms of therapy, it was felt that the drug showed sufficient promise for it to be used in a larger number of patients.

To date, perphenazine has been used in 145 male and female in-patients, the maximum period of treatment with the drug so far being 220 days. Recently admitted patients who were given perphenazine immediately after treatment with E.C.T. or I.C.T. were excluded from this assessment, because of the difficulty in determining the treatment responsible for improvement.

The patients were classified in the following groups, manic-depressive psychoses (6); schizo-affective states (4); schizophrenia (124); psychopathic personality (2); and organic and other psychoses (9). The groups were subdivided as shown in Charts A and B.

CHART A

Classification (Acute)	Total		Worse		Not Improved		Slightly Improved		Moderately Improved		Much Improved	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Manic Depressive Psychosis:												
Mania	—	1	—	—	—	—	—	—	—	1	—	—
Depression	—	3	—	—	—	1	—	—	—	1	—	1
Schizo-affective State	1	—	—	—	—	—	1	—	—	—	—	—
Schizophrenia:												
Simple	—	—	—	—	—	—	—	—	—	—	—	—
Hebephrenic	2	—	—	—	—	—	—	—	1	—	1	—
Catatonic	—	—	—	—	—	—	—	—	—	—	—	—
Paranoid	2	2	—	—	1	—	—	—	—	1	1	1
Paraphrenia	—	2	—	—	—	—	—	—	—	2	—	—
Organic and Other Psychoses:												
Senile and arteriosclerotic states ..	1	1	—	—	—	—	—	1	1	—	—	—
Epileptic psychosis	—	1	—	—	—	—	—	—	—	1	—	—
G.P.I.	—	—	—	—	—	—	—	—	—	—	—	—
Disseminated sclerosis	—	—	—	—	—	—	—	—	—	—	—	—
Psychopathic Personality	2	—	—	—	2	—	—	—	—	—	—	—
Total	8	10	—	—	3	1	1	1	2	6	2	2

CHART B

Classification (Chronic)	Total		Worse		Not Improved		Slightly Improved		Moderately Improved		Much Improved	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Manic Depressive Psychosis:												
Mania	1	—	—	—	—	—	—	—	1	—	—	—
Depression	—	1	—	—	—	1	—	—	—	—	—	—
Schizo-affective State	3	—	—	—	1	—	1	—	1	—	—	—
Schizophrenia:												
Simple	2	1	—	—	1	1	1	—	—	—	—	—
Hebephrenic	20	13	—	2	3	7	4	1	7	3	6	—
Catatonic	10	2	—	1	4	—	5	—	—	—	1	1
Paranoid	31	20	—	4	13	9	4	—	7	5	7	2
Paraphrenia	2	15	—	4	1	4	—	2	—	2	1	3
Organic and Other Psychoses:												
Senile and arteriosclerotic states ..	—	—	—	—	—	—	—	—	—	—	—	—
Epileptic psychosis	—	4	—	—	—	3	—	—	—	1	—	—
G.P.I.	—	1	—	—	—	1	—	—	—	—	—	—
Disseminated sclerosis	—	1	—	—	—	—	—	1	—	—	—	—
Total	69	58	—	11	23	26	15	4	16	11	15	6

Clinical response, which was evaluated by the medical and nursing staff in charge of the individual wards, was recorded under the following headings: worse, not improved, slightly improved, moderately improved and much improved. In those patients who were subsequently discharged on maintenance therapy the opinions of relatives concerning lasting improvement were taken into account in the assessment.

Technique of Treatment

The dosage of perphenazine was 4 to 8 mg., three times a day, increased when necessary in certain patients to 48 mg. daily. In general an effective therapeutic dosage was 8 mg. three times a day. Most of the patients who were subsequently discharged were maintained on a dosage of 4 mg. three times a day.

Chronic cases had been in the hospital for over one year and up to 42 years and had received all routine forms of therapy including chlorpromazine, reserpine, E.C.T. and I.C.T. and, in some cases, leucotomy.

The acute cases were those who at the time of this drug assessment had been admitted to the hospital less than a year but more than six months ago. All had received other treatment within the last six months, for example, reserpine, chlorpromazine, or other phenothiazines, E.C.T., and I.C.T. Any response to these forms of treatment had been limited, and perphenazine was then administered.

In all cases the time lapse since I.C.T. or leucotomy was sufficient to discount a delayed response, and the results of E.C.T. or drug therapy had not been satisfactory.

Side-Effects

Parkinsonism was the most frequent physical complication, occurring in all grades of severity from slight tremors to severe manifestations of the typical syndrome. Oculogyric crises, in one instance accompanied by moderate tremor, appeared in two women. In one of these cases the drug was later started again and increased to double the original dose, but again had to be stopped when a further crisis occurred. In 5 cases in which Parkinson-like symptoms supervened, cessation of treatment for 48–72 hours with a subsequent increase to the original dose was not attended with a return of Parkinsonism: but in other cases this manoeuvre was not successful. Parkinsonism generally emerged with a lower dosage in females, but as a dose of 24 mg. was not exceeded on the female side this impression was not fully tested. Six women who developed Parkinsonism were given concurrently Disipal or Artane with definite relief. A suggestion that very long-standing schizophrenics might be less likely to develop the syndrome was not sustained on analysis. During the trial there was a clinical impression that the maximum therapeutic dose was one which produced Parkinsonism, and bearing in mind the reservation on the female dosage an analysis might give some support for this assumption. Thus, if all improvements are placed together and the not improved and worse cases are combined, the following figures emerge:

		Male	Female	Total
Parkinsonism:	Improved	20	11	31
	Not improved	6	5	11
No Parkinsonism:	Improved	30	19	49
	Not improved	19	33	52

However, good improvements were obtained in both groups, and the most one can deduce is that in some cases improvement does not occur unless the drug is given at a dose which will produce Parkinsonism in that person. Fortunately in most cases suffering from this side-effect, it was possible to reduce the dose, after improvement had been secured, to a level at which Parkinsonism did not occur yet improvement was maintained. The onset of Parkinsonism varied from the third day at 12 mg. daily to the seventh month at 36 mg. daily. One male patient had a disturbing protrusion of the tongue, and four women, included in this group, on questioning about their health, complained of aching legs though other features of the syndrome were absent. In 4 instances on the female side treatment was stopped because of this complaint.

Restlessness of a compulsive type was very common, the patient feeling that he had to keep marching up and down. Two women experienced vaso-vagal attacks, both occurring on a very hot, close day. No other instances of a disturbance in blood pressure were observed. One woman had to stop the drug because of gastric pain and nausea. No cases of jaundice occurred.

In seven instances on the female side the drug was stopped because of a deterioration in behaviour, which made their nursing a serious problem in an overcrowded ward with many potentially troublesome patients. Along with the four women whose treatment was stopped because of Parkinsonism, they were classified as having been made worse by the drug. In actual fact all of these cases showed a striking reversion to the symptoms and signs they had displayed at the time of admission.

On the male side a number of cases also showed a "reactivation of the psychosis" and here the patients were treated with increasing doses of the drug, a good improvement being secured in all instances. Thus it would appear that such reactions respond well to resolute therapy if ward conditions permit such a course.

Therapeutic Results

In the male group of 69 chronic cases, 46 (66 per cent.) improved to some degree and the improvement was substantial in 31 of these. In the female group of 58 chronic cases, perhaps for reasons already stated, only 21 (36 per cent.) showed improvement, 17 of them of moderate or marked degree.

In the male group of 8 acute cases, 5 (62 per cent.) showed improvement and in the female group of 10 cases 9 (90 per cent.) improved.

Altogether 4 women and 8 men were discharged and several others are under consideration for early discharge or trial.

It is always difficult to assess accurately the exact contribution of a drug when improvement has occurred, but the selection and nature of the cases led us to believe that where improvement occurred it was due to perphenazine. The response was related to the giving of the drug and the number responding was greatly in excess of what could be expected in the normal course of events. Most patients had been subjected to previous drug trials, group training and attempts at rehabilitation. In those patients showing improvement, treatment was continued long enough to exclude the factor of optimism and to pass through the reaction of disillusionment. Conditions in some wards were being improved, in others had already been improved, yet there was no significant variation in the patients not attributable to more potent causes. Apart from those cases where the drug was stopped for behaviour or physical reasons, six cases were stopped at between 3 and 4 months because they were showing no improvement. One case at 3½ months suddenly started to improve, the improvement progressing to the highest category, and it may be that a few cases will improve if continued for four months or even longer. In the majority, improvement set in during the first four weeks, and in many instances in the first week.

It was noted that, in general, patients who had been leucotomized responded less well and the following analysis shows this graphically.

Sex		Worse	Not Improved	Slightly Improved	Moderately Improved	Much Improved	Total
Female	..	2	5	1	2	—	10
Male	..	–	6	8	1	—	15

The decision to perform this operation implies a rigorous selection of the least responsive to other forms of treatment and too much should not be read into these results. In no instance did the drug appear to heighten epileptic activity.

An analysis of the results in relation to the duration of the illness was made when the following emerged:

Years		Worse	Not Improved	Slightly Improved	Moderately Improved	Much Improved	Total
1– 2	..	–	–	2	1	3	6
2– 5	..	1	4	2	8	7	22
5–10	..	4	13	4	8	7	36
10–15	..	1	12	4	6	1	24
15–20	..	3	2	1	1	1	8
20–25	..	–	5	–	3	2	10
25–30	..	1	7	4	–	–	12
30+ ..	..	1	6	2	–	–	9

It is realized that the numbers involved are too small to merit any conclusions, but it was considered that the number of improvements in cases hospitalized for as long as 24 years was startling and far in excess of those previously obtained by drug or other treatment at this hospital. Even slight improvements in cases of this duration, in the form of increased interest and general awareness, behavioural and toilet improvement, speech and co-operation, especially where these cases had been resistant to other forms of treatment and had shown no natural fluctuation in the disease process, were thought to be a remarkable achievement.

A particularly gratifying feature was the response in some patients in the paranoid group. These cases occurred in both the schizophrenic and paraphrenic groups and were characterized by sustained touchiness, suspiciousness, arrogance, hostility, querulousness, litigiousness and hypochondriasis with a well-retained personality. Within a few days of starting the drug these patients lost their "sting" and became benign, friendly, co-operative, and considerate. Many declared they had never felt better and could describe clearly their mental comfort and freedom from suspicion and delusional thinking. A few proceeded to gain a degree of insight such as we have never seen in these patients with any other drug or treatment. Such patients were willing to ascribe their improvement to the drug, a fact which augurs well for the continuance of maintenance treatment after discharge, and this has been supported in those cases so far followed up. In other cases there is recovery or improvement without insight, and the only discharged case who has stopped taking his treatment falls into this category. There is also the possibility that improvement with the drug permits of more convincing dissimulation. On the day after this review was completed a female paranoid schizophrenic patient with a malignant heredity and history, who had been put in the moderately improved category, and who had appeared in good spirits and looking forward to a visit from her sister that afternoon, broke her grounds parole and committed suicide. This case deserves especial mention, since, in view of her history, the medical and nursing staff had been extraordinarily cautious and painstaking in the management of her case and in assessing her progress.

CASE HISTORIES

Case 1

M.W., aged 39. This woman, whose husband is now separated from her, was first admitted to this hospital in August, 1957 suffering from paranoid schizophrenia. She was admitted for the third time on 20.9.58. Then she was hallucinated, believed that people were spreading lies about her associating with men, accused the Welfare Officer of slandering her, thought her neighbours were persecuting her and that the Masons were taking advantage of her. She was a difficult nursing problem, readily becoming quarrelsome and aggressive if frustrated in any way. Previously she had been treated with E.C.T. and chlorpromazine, failing to continue her tablets after discharge. On this occasion she was treated with massive reserpine, on which her behaviour improved though her basic paranoid delusions remained unchanged. On 5.1.59 without warning she broke her grounds parole and was later found in her home having attempted suicide by lysol poisoning.

On 11.2.59 she was put on Fentazin 12 mg. daily with an almost immediate marked improvement. She no longer showed signs of psychosis, but had no insight. She was a pleasant, easy, co-operative patient, loud in her praises of the drug. Her improvement was maintained and she was eventually discharged, after 28 days' trial, on 12.6.59, her doctor being advised to continue her on 12 mg. Fentazin daily.

Case 2

M.M., aged 39. This married woman first developed paranoid schizophrenia 7 years ago and had twice been admitted to this hospital before her present admission in April, 1956. She was aurally hallucinated, believed she received messages over the wireless and heard men making improper suggestions to her in the streets, expressed the belief that her husband was unfaithful and was trying to poison her, entertained numerous sexual delusions, and believed that an attempt was going to be made to kill her. Previously treated with E.C.T. she was given a course of deep insulin with temporary improvement. On chlorpromazine she improved without insight but when put on trial she stopped taking her tablets and returned as bad as ever. The same occurred when reserpine was exhibited. Her personality was well retained and she was a great nursing problem, being touchy, suspicious, quarrelsome, disputatious and litigious, arrogant and aggressive.

Fentazin, 12 mg. daily was commenced on 21.2.59, with almost immediate improvement. Her psychotic symptoms were no longer evident, she denied her former delusions, was pleasant and co-operative, lost her arrogance and touchiness, stated she had never felt better and ascribed this improvement to the Fentazin. Her basic paranoid attitude is still evident when she is confronted with difficulties, but we have never seen her better and arrangements are being made for a further trial at home.

Case 3

R.D., aged 39. This man first became ill in 1943 with paranoid schizophrenia. In 1944 he was treated with cardiazol and discharged after three months. He was re-admitted in 1948, recovered with I.C.T. and was discharged nine months later. In 1951 he was admitted to another hospital and was discharged in 1957 following improvement with reserpine.

In August, 1958 he was re-admitted to this hospital with florid paranoid symptoms despite the fact that he had continued on his reserpine. A course of E.C.T. was given and again he was put on reserpine. Despite the latter he relapsed again in November, 1958. Reserpine was eventually terminated on 13.1.59 and Fentazin commenced, increasing to 28 mg. daily after 7 days, and dropping again to 12 mg. daily after a further 19 days because of the development of Parkinsonism.

Improvement commenced almost immediately and in April his mother stated "He was never so well as he is now, He is helpful and considerate. Before he was inconsiderate as if he didn't care, as if he had no feeling for you. He would seem to be angry with me for no reason. Since you changed his medicine his restlessness and his bad temper have stopped. He has been well ever since. Everyone has remarked at the difference. It's amazing, knowing what he was like—you can hardly think he's the same person."

He was discharged in May, 1959 at which time he remarked—"When I came into hospital I believed that everyone was against me. There was no coherent explanation for this feeling. I am no longer obsessed now with looking for evidence that people are against me." He left on a maintenance dose of 12 mg. daily.

Case 4

K.McP., aged 37. This man suffers from paranoid schizophrenia of at least 10 years' duration, characterized by visual and aural hallucinations, grandiose Messianic delusions with persecutory expressions, depression and hypochondriasis. He has been treated with E.C.T. on several occasions, I.C.T., chlorpromazine, azacyclonol and reserpine with only slight or temporary improvement.

Treatment with Fentazin was commenced on 21.12.58 the dose being increased gradually to a maximum of 24 mg. daily and subsequently maintained at 12 mg. daily since 18.3.59. Since then he has been free from hallucinations, delusions and hypochondriasis, and, although he is still lethargic, solitary and lacking in drive, he now employs himself in the hospital, avails himself of grounds parole, and is a pleasant, easily managed patient.

Case 5

J.G., aged 23. This man was admitted on 24.3.58 under certificate. There is a bad family history and he had previously been solitary, dreamy and moody. Two months prior to admission he suddenly became excited and disturbed in his behaviour, claimed that God had given him the gift of curing people, attended Church frequently and expressed a desire to make sacrifices. He was later arrested for getting into a car, claiming that it was his own and refusing to leave. On admission he was in a state of catatonic stupor, mute and negativistic.

Two courses of E.C.T. and a course of 50 insulin comas produced no real improvement and on 1.10.58 he was transferred to a chronic ward giggling incessantly and living in his own private world.

Fentazin was commenced on 7.3.59 increasing in two weeks to 36 mg. daily and at this dosage there was an immediate and dramatic improvement, the only evidence of his illness being a slight woolliness in thinking and a mild degree of facial grimacing. He employed himself in the hospital and mixed with other patients and was able to have leave from the hospital. Because of a moderate degree of tremor his dose was reduced but he appeared less well mentally and he was restored to 36 mg. daily. He was able to leave hospital on this dose on 11.7.59.

Case 6

R.R.W., aged 38. This man has suffered from a paranoid schizophrenic illness for eight years and had failed to respond to a course of 60 insulin comas, E.C.T., chlorpromazine or reserpine. He commenced Fentazin on 23.12.58, the dose being increased to 28 mg. daily and finally reduced to a maintenance dose of 12 mg. daily as from 23.4.59. A mild degree of Parkinsonism developed on the maximum dose but disappeared on dropping to the maintenance dose.

Improvement set in a few weeks after the start of the treatment and he has now been free from florid psychotic symptoms for five months and discharge is being considered.

An intelligent man, he wrote the following observations on Fentazin therapy—"When I first became ill I was in a state of depression, and found my mind constantly cluttered up with thoughts, some pleasant, some not so pleasant. According to what was taking place around me then, I came to a conclusion I was involved in some large plan specially arranged by people of influence. I looked for an explanation of this plan and soon found myself convinced that it must involve the several people of distinction I had met during the war. Several incidents in the past relating to these people enabled me to satisfy my reasoning. If a black cat crossed my path I would be on the lookout all day for good luck to justify this having been planned. If a shop said they did not have my favourite brand of tobacco and offered me an inferior brand I thought they were purposely trying to make things difficult. This led to ideas of persecution and suspicion, for if things were becoming difficult, I would attribute it to people in the plan. I thought it was all done to annoy or persecute me, and part of the plan . . .".

"The effect that Fentazin had on all this has been to stabilize my physical and mental condition, so much so that I now tend to put trivial things in their proper perspective, and am not troubled by ideas of association or of persecution, if they present themselves."

Case 7

G.S., aged 13. This boy was admitted on 17.1.59. His mother is a patient in the hospital suffering from a paranoid psychosis. An only child, he was considered to be mentally retarded at the age of 5 years, his I.Q. being estimated as 61. He was then noted to be immature for his years, restless and "always on the go". He was transferred to a special school and then to an occupational centre because of his restlessness. Later he was reported to be excitable, highly strung, restless and facile. In 1956, when his mother was admitted to this hospital, a headmaster reported that he was boisterous, silly, noisy and did not profit from experience. Shortly before admission he caused a breach of the peace by "his stupid behaviour" and was referred once more to the psychiatrist who advised admission to hospital as he felt that the boy was hallucinated and suffering from schizophrenia.

On admission he was excited and elated, restless and hallucinated. He stated he was a Communist spy, that he hated the Scots and wanted to kill people, cut off their heads. "I love wars—fighting and cheering down the streets with a lot of bottles like a gangster—I think Rubina Frankenstein was going to rape me—I think she is going to stick pins in my father's back." Some of his delusions were similar to those expressed by his mother but many were original. Psychological investigation was carried out on the Revised Stanford Binet Scale and the Wechsler Intelligence Scale for children and also the Rorschach Test. His I.Q. was assessed at 58 and 47 but there was considerable scatter on the subtests, and general disorganization of thought. He was considered to be suffering from schizophrenia and subsequent observation supported this diagnosis as he became more overt in his behaviour, shouting back in response to his aural hallucinations, covering his food to prevent it being poisoned, giggling and laughing for no reason.

On 17.2.59 he started a course of 10 E.C.T. modified by Scoline. This produced a transient improvement. On 1.4.59 he was put on Fentazin 2 mg. t.i.d. and this was gradually increased to 8 mg. t.i.d. on 27.4.59, and finally to 32 mg. daily on 6.7.59. At this dose he was no longer hallucinated and was able to be on grounds parole and to work with the garden squad, though he continued to assert that he hated the Scots and would like to be a Russian.

Case 8

W.H., aged 29. This man has suffered from hebephrenic schizophrenia for 9 years. He was treated in another hospital with E.C.T., I.C.T. and reserpine. On the latter treatment he improved and was discharged in October, 1958. Unfortunately he stopped taking his tablets and was admitted to this hospital on 9.2.59 at which time he was woolly, blunted, manneristic and resistive, and his conversation was completely disorganized. Fentazin was commenced on 12.2.59 and increased to 48 mg. daily on 4.4.59. A month after the start of Fentazin he commenced to improve and since April he has been very well. His conversation is rational, he shows no psychotic signs, he keeps himself clean and tidy, is pleasant and co-operative and is able to enjoy grounds parole, and to go home unaccompanied on day pass.

Case 9

N.K., aged 22. This man was admitted on 7.10.58. At the age of 10 years the parents had been advised that he was backward and should go to a special school but refused to accept either the diagnosis or the advice. From the age of 15 his behaviour deteriorated steadily. He became restless and overactive, would jump on chairs and other furnishings, and dismantled things like the radio and his bicycle. He then became violent, threw a child over a fence and two years ago started to attack his mother accusing her of poisoning his food. He complained of hearing trains at night and then of hearing voices and of a smell coming from him. He often smiled to himself.

On admission he was withdrawn, emotionally blunted and fatuous, uncommunicative and lacking in rapport. He was considered to be suffering from hebephrenic schizophrenia. Psychological testing established his present I.Q. at 62, but his test behaviour supported a diagnosis of a well-established schizophrenic illness with no current florid production.

There was no improvement with conservative treatment and Fentazin was commenced on 22.1.59 and raised gradually to 36 mg. daily. At this level he developed a mild Parkinsonism and the dose was reduced. Within a few weeks of commencing treatment there was a marked improvement and since then he has been able to employ himself, to have grounds parole and week-end leave, is sociable and able to mix with others, and is now being considered for discharge.

COMMENT

Whilst this review has of necessity been limited in its scope, and the numbers in categories, other than the schizophrenic and paraphrenic groups, too few even to indicate trends, it was felt that a preliminary report was warranted.

At the present stage it would seem reasonable to conclude that perphenazine is the most potent drug we have used in the treatment of schizophrenia and paraphrenia. A point of interest and importance is that a reasonable number of hebephrenic as well as paranoid schizophrenics were materially benefited by it. The less satisfactory result in catatonic and simple schizophrenia does not indicate that it is necessarily ineffective in these conditions, but further experience is required. The number of improvements in long-term, hospitalized patients, previously resistant to other treatments, was surprising and especially encouraging.

It was encouraging also to find that so many of the patients who improved were prepared to give the credit to "the tablets" and were agreeable to continue the suggested maintenance dose when discharged. In the case of other drugs we have tried this has not been experienced, and the number of patients who failed to continue their treatment and had to return to hospital was so high that one tended to become sceptical of the overall benefit of these drugs.

In view of these features it is felt that there is a definite place for the use of perphenazine in psychiatric practice and for a wider investigation of its potentialities.

In conclusion we would like to thank Dr. A. P. Russell, the Physician Superintendent, and Dr. M. Devlin, Deputy Physician Superintendent, for their guidance and encouragement during the investigation and in the preparation of this paper, and also Messrs. Allen & Hanburys for a generous supply of the drug.

SUMMARY

The clinical effects of perphenazine therapy were observed in 145 male and female patients with a variety of psychiatric conditions.

In the male group of 69 chronic cases 46 (66 per cent.) improved. In the female group of 58 chronic cases 21 (36 per cent.) improved.

In the male group of 8 acute cases 5 (62 per cent.) improved. In the female group of 10 acute cases 9 (90 per cent.) improved.

The dosage of perphenazine varied from 24 mg. to 48 mg. daily and in most cases a maintenance dose of 12 mg. daily was finally achieved.

It was considered reasonable to ascribe the improvements achieved to perphenazine.

Perphenazine is a useful addition to psychiatric therapeutics.

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DIMENSIONS OF PERSONALITY, PSYCHIATRIC SYNDROMES, AND MATHEMATICAL MODELS

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I. INTRODUCTION

It is well known that psychiatric diagnostic groupings have no claim to represent any fundamental scientific causal principle, but reflect rather the needs of administrative convenience and compromise between different theoretical orientations (Eysenck, 1960). Doubt has in fact been expressed regarding the advisability of retaining categorical divisions in a field where quantitative differences along orthogonal dimensions may be more appropriate than qualitative differences between distinct disease groups (Eysenck, 1947). The appropriate statistical method for dimensional analysis is, of course, multiple factor analysis (Eysenck, 1952) and it is possible to show relationships between factors or dimensions and psychiatric categories by giving factor scores to the subjects of the experiment and to average these scores for groups of subjects sharing a common diagnostic label (Eysenck, 1959). In this way it has been demonstrated that along the dimension of extraversion/introversion, subjects diagnosed as psychopaths tend to have particularly high extraversion scores; hysterics tend to be extraverted but not as highly as psychopaths. Patients suffering from one of the dysthymic conditions (anxiety, reactive depression, obsessional disorders), tend to have high scores on introversion. Mixed neurotics tend to be in between the other groups. All these diagnostic groups have high scores on the factor of neuroticism which is orthogonal to extraversion/introversion (Eysenck, 1957).

In recent years a new method has come to the fore which is particularly concerned with the analysis of differences between groups. This method is sometimes referred to as "canonical variate analysis", but more fittingly perhaps, the canonical analysis of discriminance. This is an extension of principal component analysis to the variation of observed differences between groups in a multi-dimensional space. Leaving out all technicalities the purpose of this method may be briefly described as follows. Assume that we have g groups and that the members of these groups have been administered m tests. We find first the mean combination of the scores on the m tests which achieves the maximum discrimination between the g groups. We then go on

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* We are indebted to the U.S. Army for the support of this investigation under contract number DA–91–508–EUC–311. S. B. G. Eysenck also acknowledges support from the Bethlem-Maudsley Research Fund. The authors wish to acknowledge the co-operation of Colonel J. McGhie, commanding officer of the Royal Victoria Hospital, Netley, who allowed the patients under his charge to act as subjects for the research.

to find another combination of the m scores orthogonal to the first which maximizes the residual differences between the g groups. A third, fourth, etc., combination can be added, provided that the appropriate test of significance does not indicate that these further combinations do not add any true variance. The number of significant combinations indicates the dimensionality of the group/test combination, the only proviso being that this is a minimal and not a maximal estimate*. Applications of this method in psychology have mainly been devoted to the problem of whether psychoses and neuroses are independent dimensions or whether psychotic disorders are merely more severe expressions of the same underlying disorder as neuroses (S. B. G. Eysenck, 1956; Eysenck, 1955). In one case the analysis has been applied to the dimensionality of neurotic groups (Slater, 1947), and in another application has been made to a psychosomatic problem (Hamilton, 1950). Little has been learned about the relationship between these two methods of analysis and except for a recent theoretical and experimental paper by Slater (1960), psychologists have been left without much guidance in this matter. It is not clear under what conditions one method would be preferred to the other, and it is not always clear whether similar or different results would be expected from the use of these two methods.

Certain points are, of course, obvious. If the allocation of subjects to groups is very unreliable, or where such allocation is irrelevant to the theoretical purpose of the analysis, canonical analysis of discriminance is not to be recommended. Under conditions where reasonable reliability of allocation is present and where the relative positions of the groups and their dimensionality are relevant to the hypothesis under investigation, canonical analysis of discriminance may have considerable advantages over factor analysis in parsimony of underlying assumptions and in various other ways.

As regards a comparison between the results to be expected from the two methods, again certain points are fairly obvious. Dimensions may emerge in a factor analysis which have no counterpart in canonical analysis of discriminance, simply because the groups selected did not reflect this dimension or are in fact chosen in such a way as to rule out the influence of this factor. If we give a battery of tests to groups of hysterics, dysthymics, normals and psychotics, which have been equated for intelligence, then a canonical analysis of discriminance of these groups will not furnish us with evidence regarding the existence of the dimension of intelligence, whereas a factor analysis would do so. Quite generally Slater, in his examination of the mathematical principles underlying these methods came to the conclusion that the axes or dimensions defined by canonical analysis of discriminance "do not necessarily coincide with those found by factor analysis of the same data. There are no *a priori* reasons for expecting the most significant differences to appear in the dimensions where the variance of the individuals about their group means (or about the general mean for all groups) is widest."

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* Slater (1960) puts the technical points involved most succinctly: "Canonical analysis is applicable to the measurements obtained by giving a number of psychological tests to individuals belonging to several groups. The means of the g groups form a scatter of g points in the m-space defined by the m tests, which is the dispersion between groups. The individuals' scores form scatters about their group means which can be collected to form a dispersion within groups. When the two dispersions are contracted simultaneously to the extent necessary to normalize the variance within groups in all dimensions, the between-group dispersion assumes an ellipsoidal form in a D-space which may be m-dimensional or less. Its major axis is the dimension where the most significant differences between groups are to be found, the next the dimensions where differences independent of the first are most significant, etc. The canonical analysis of discriminance is a principal components analysis applied to this contracted dispersion between groups to define its axes and test the significance of the variation there."

There are, however, conditions under which good agreement in certain respects may be expected and is indeed required by the hypothesis under investigation. This is true in particular when a battery of tests has been chosen on a rational basis to mediate the measurement of one dimension, and where groups have been chosen in such a way that rational predictions can be made from the same theory regarding their respective positions. Under these conditions, and provided that the theory is in fact correct, we would expect one dimension to emerge from the canonical analysis of discriminance, which would be similar to one specific factor emerging from the factor analysis. Such coincidence would give particularly strong support to the hypothesis under investigation because the assumptions made by one method, both mathematical and theoretical, are different from those made by the other, and coincidence would only be achieved if these assumptions were in fact justified.

II. Analysis

The data here analysed were originally collected in connection with a factorial study of extraversion/introversion by Claridge (1960). The tests used in this study were specially chosen in order to test the theory put forward by one of us postulating excessive reactive inhibition and satiation in extraverts and defective reactive inhibition and satiation in introverts (Eysenck, 1957). A number of predictions were made from this theory which have been tested experimentally at various times. Thus, it was predicted that reminiscence would be greater for extraverts than for introverts, in accordance with the well-known hypothesis that reminiscence is due to the dissipation of reactive inhibition accumulated during massed practice. Similarly, it was predicted that the after-effects of observing a rotating spiral would be more protracted for introverts than for extraverts, due to satiation of the underlying physiological processes. In regard to vigilance tests, it was predicted (*i*) that extraverts would show a greater fall off in performance with time, due to the accumulation of more reactive inhibition and (*ii*) that the introduction of a novel stimulus after a considerable degree of inhibition had been reached on the vigilance task, would lead to (*a*) inhibition of performance for introverts, and (*b*) dis-inhibition and consequently improvement of performance in extraverts. In relation to another experiment yet, namely time error, it was argued that the application of the first of a pair of stimuli would produce, in addition to the expected excitatory effect, an inhibitory process opposing the continuation of this excitation. A variable stimulus of equal intensity would then be judged greater, according to the degree to which inhibition consequent upon the first stimulus had damped down the original excitation. Extraverts, producing more inhibition as a result of the first stimulus, would be expected to show a greater tendency towards negative time errors than introverts.

Tests of this kind were given to 16 hysterics, 16 dysthymics, 16 psychotics and 16 normal subjects, all of them of roughly equal age and intelligence. Subjects were selected for these groups in terms of considerable psychiatric agreement on diagnosis. A factor analysis was performed by Claridge on 30 scores altogether; in view of the possible disrupting effect on psychotics, whose performances tend to be rather erratic, the factor analysis of the complete set of scores was repeated by using only the 48 subjects in the normal and neurotic groups and excluding the psychotics. In both analyses four factors were extracted, accounting for almost 50 per cent. of the total variance. Three of these factors are of little concern in this connection, but the fourth one was clearly identified as extraversion; this factor had high loadings on such measures as the vigilance test (performance), vigilance test (effect of novel stimulus), spiral after-effect, reminiscence, time error, and the extraversion scale of the Maudsley Personality Inventory (Eysenck, 1959).

By and large, this research suggested that the theory underlying the selection of tests was correct, at least in part. The research did, however, leave open the possibility that that part of the hypothesis relating to the selection of groups might be mistaken. In other words, it is conceivable that hysterics and dysthymics might not emerge as the most extraverted and introverted groups respectively with regard to this factor, and the present paper presents an attempt to answer this question in two ways. (1) By the calculation of factor scores, and (2) by the calculation of canonical variates. In addition, of course, our interests will lie in a comparison of these two quite dissimilar methods of analysis.

Our method of estimating factor scores follows that of Thurstone, and two sets of factor scores were in fact calculated, derived from the two analyses mentioned above, i.e. with and without the inclusion of the schizophrenic group and deriving respectively from the 64 and 48 subjects. Mean factor scores and sigmas are given in Table I. It will be seen then that on both accounts the dysthymic groups have the lowest score on extraversion (—3·44 and —4·07 respectively), while the hysterics have the highest scores (2·27 and 2·08 respectively). The difference between the groups is about twice the size of their standard deviations, and as predicted normals and psychotics are intermediate. These results strongly support the hypothesis that the psychiatric groups do in fact represent extremes along the dimension of extraversion/introversion.

TABLE I

Factor Analysis

Factor Scores: (64) Extraversion Factor

	N:	D:	H:	P:
Mean	1·98	—3·44	2·27	1·14
σ	2·35	1·38	1·94	2·64

Factor Scores: (48) Extraversion Factor

	N:	D:	H:	P:
Mean	1·99	—4·07	2·08	—0·16
σ	3·09	2·37	3·06	3·55

We must next turn to the canonical analysis of discriminance. Two such analyses were in fact carried out, making use of two different sets of five tests each. Each set included, as well as measures of extraversion/introversion, two tests of neurotic and psychotic abnormality, as it was thought that in this way we could assure the presence of a significant second canonical variate which would add to the interest of the analysis. The tests used are given below:

Group 1:

A1. Number of sortings on the Payne (1960) sorting test of schizophrenic thought disorder.
A2. Total score on the first part of the vigilance test.
A3. Mean length of after-effect on four trials of the rotating spiral test.
A4. Total amount of sway on the body sway test of suggestibility.
A5. Time error.

Group 2:

B1. The logarithm of the time taken on the Payne (1960) sorting test.
B2. Change on the vigilance test as a result of introducing a novel stimulus.
B3. Time judgment, i.e. judgment of elapsed time under standard conditions.
B4. The neuroticism part of the Maudsley Personality Inventory.
B5. Improvement on the pursuit rotor during the third five-minute trial. (The three trials were separated by two rest pauses of ten minutes each.)

The tests were chosen so as to give a fairly representative selection of different measures but no account was taken of the factor analysis as this had not been completed when the tests were chosen for the canonical analysis of discriminance. It would be possible now to select a group of tests having higher factor loadings than the ones actually chosen. The extraversion scale of the Maudsley Personality Inventory, while it has one of the highest factor loadings on Extraversion, was excluded from consideration as our main interest lay in *performance* tests of extraversion.

III. RESULTS

Table II shows three latent roots extracted on the first set of tests; Table III shows the latent roots extracted from the second set of tests. Both sets agree in finding two significant latent roots; the third one falls short of significance in both analyses. Tables IV and V list the mean scores from the three canonical variates which are obtained by using the latent vectors as weights and multiplying them by the scores on the tests. (The third latent root has been retained for the sake of interest in spite of its failure to achieve statistical significance. This fact should be borne in mind in the subsequent discussion.)

TABLE II

Latent Roots

A

$\lambda_1=0\cdot337{,}973$ (56·730 per cent.)	P<·01
$\lambda_2=0\cdot213{,}797$ (35·886 per cent.)	P<·02
$\lambda_3=0\cdot043{,}989$ (7·384 per cent.)	P=N.S.

TABLE III

Latent Roots

B

$\lambda_1=0\cdot578{,}292$ (62·372 per cent.)	P<·001
$\lambda_2=0\cdot231{,}140$ (24·930 per cent.)	P<·01
$\lambda_3=0\cdot117{,}740$ (12·699 per cent.)	P=N.S.

On the first variate dysthymics have the highest scores and hysterics and psychotics have low scores; in the second analysis, dysthymics again have the highest scores and hysterics share the distinction of having the lowest scores with the normals. Individually the two analyses agree in singling out the dysthymics from the rest but in the one analysis the hysterics have almost identical scores with the psychotics, in the other, with the normals. As will be shown later a combination of the two analyses gives a perfect fit to our hypothesis.

TABLE IV

Mean Group Variate Scores

A

	N:	D:	H:	P:
$\bar{\gamma}_1$	35·224	41·566	27·724	26·124
$\bar{\gamma}_2$	−1·028	5·203	−0·236	6·866
$\bar{\gamma}_3$	12·024	19·860	22·559	14·746

TABLE V

Mean Group Variate Scores

B

	N:	D:	H:	P:
$\bar{\gamma}_1$	−6·353	−41·716	−11·895	−23·815
$\bar{\gamma}_2$	46·350	48·656	55·885	59·716
$\bar{\gamma}_3$	38·822	34·240	28·922	40·761

As regards the second variate we find that psychotics have the highest score in both analyses, while normals have the lowest; this is possibly to be interpreted by regarding the second variate as an approximation to the factor of psychoticism (Eysenck, 1952).

As regards the third variate, which it will be remembered did not achieve significance, we find that the two neurotic groups are opposed to the normal and the psychotic groups in both analyses. This congruence suggests that here we are dealing with a variate which is similar to the factor of neuroticism in several factor analytic studies (Eysenck, 1959). The fact that the latent roots are not significant speaks against taking them too seriously, but the agreement between the two analyses may make us incline to regard this outcome as probably non-chance. Tables VI and VII indicate the percentage of misclassification if subjects are graded according to their canonical variate scores, and this grading compared with diagnoses. It will be seen that the total percentage of misclassifications is on the average about 23; this is not a bad result considering that only one test each was included for the psychotic and neurotic dimensions and even these were not selected as being the best available. In group A, of 16 patients diagnosed as dysthymic, none were graded with hysterics, in terms of the test results; in group B the same result was found. Of the 16 hysterics one and none respectively were graded as dysthymics in terms of test results. Thus, the comparison between the two groups which are central to our study discloses only one false classification out of 64 possible errors.

TABLE VI

Diagnosis

A

	N	D	H	P
N	*13*	1	5	1
D	2	*12*	1	1
H	1	0	*10*	2
P	0	3	0	*12*
	16	16	16	16

26·6 per cent. misclassification

TABLE VII

Diagnosis

B

	N	D	H	P
N	*14*	0	2	3
D	0	*14*	0	0
H	1	0	*13*	2
P	1	2	1	*11*
	16	16	16	16

18·35 per cent.
misclassification

It seems desirable to combine the first canonical variates from the two analyses in order to obtain a good general estimate of individual scores, and this was done by transforming all individual scores into standard scores with a mean of 100 and standard deviations of 10; these were then added and averaged. The same was done for the second canonical variate, which has been provisionally identified as psychoticism. The results are quoted in Figure 1.

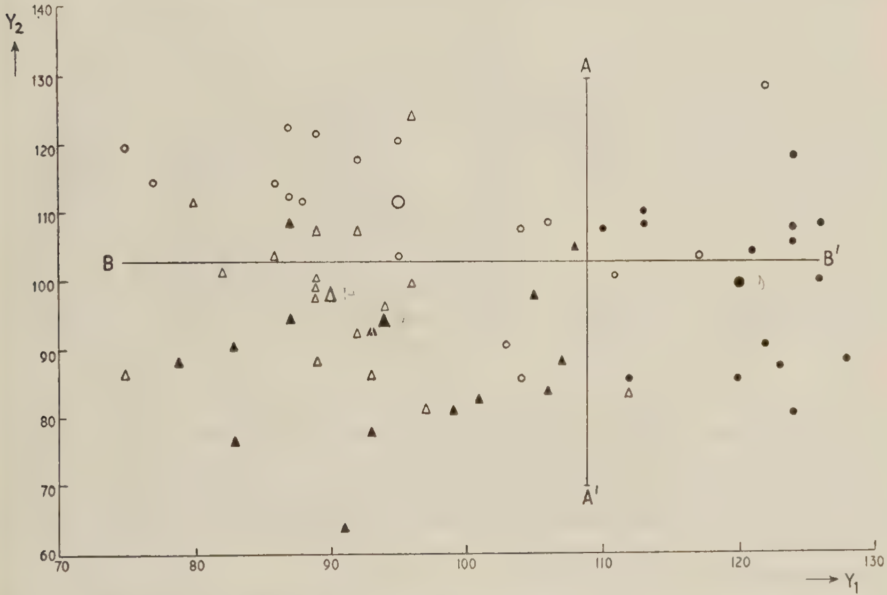

FIG. 1.—Positions of 16 normals (solid triangles), 16 dysthymics (solid circles), 16 hysterics (triangles) and 16 schizophrenic psychotics (circles) on two canonical variates. Large circles and triangles denote mean scores of respective groups.

Line A–A′ has been drawn parallel to γ_2 to show that this variate separates dysthymics from hysterics with only one misclassification; one hysteric is grouped with the dysthymics. Line B–B′ has been drawn to show the degree of separation achieved between psychotics and the other groups. Above this line there are 14 out of 16 psychotics; this success is bought at the expense of having 7 normals and hysterics diagnosed as psychotic as well as 8 dysthymics. Clearly, discrimination is best in respect of that set of groups in which our main interests lay, and for which our tests were predominantly selected.

We must next turn to a comparison of factor scores as obtained from the factor analysis with the canonical variate scores in γ_1. There is considerable agreement between these two scores; this agreement is expressed in the terms of the correlation of +0·89, when factor scores are those derived from the total group of 64 subjects. When the factors derived from the smaller group are used, correlation becomes +0·81. It is clear that the results of the two entirely different and separate analyses give very similar outcomes.

It may be of some interest to look at the table of latent vectors for the three canonical variates. These are given in Table VIII for the two sets of tests. As these values indicate the weight which each test assumes in deriving scores for the variates, we would expect by and large that those tests intended to measure extraversion would have high figures in column X_1, those tests intended to measure psychoticism in column X_2 and those tests intended to measure neuroticism in column X_3. On the whole this expectation is borne out. For X_1 the two tests having much the highest weights are A_2 and B_2, both of which were included as tests of extraversion. A_1 and A_4, tests of psychoticism and neuroticism respectively, have the lowest values on X_1; A_4 has much the highest value on X_3 as it should. A_1, however, fails to have the highest value on X_2 as predicted; it falls into second place only.

TABLE VIII

Latent Vectors

Test	Dimension Measured	X_1 (E)	X_2 (P)	X_3 (N)
A_1 Payne sorting; number of sortings	P	−0·027,547	−0·158,406	−0·205,837
A_2 Vigilance; total score	E	1·000,000	−0·026,706	0·433,846
A_3 Spiral after-effect	E	0·264,823	1·000,000	−0·284,795
A_4 Body sway	N	0·011,551	−0·057,418	1·000,000
A_5 Time error	E	0·284,756	−0·062,453	−0·136,360
B_1 Payne sorting; log. time	P	−0·309,036	1·000,000	1·000,000
B_2 Vigilance; change	E	1·000,000	0·389,368	−0·276,749
B_3 Time judgment	E	−0·177,192	−0·313,304	0·603,393
B_4 M.P.I. neuroticism scale	N	−0·698,485	0·333,239	−0·772,843
B_5 Pursuit rotor improvement ..	E	−0·193,660	0·219,790	0·279,866

As regards the second analysis, B_1 as predicted has the highest score on X_2 but also somewhat unpredictedly on X_3. B_4 which was expected to have the highest score on X_3, only has the second highest. It also has an unexpectedly high value on X_1 which is probably due to the fact that in neurotic groups B_4 (the M.P.I. neuroticism scale) shows quite high correlations with extraversion (Eysenck, 1959). By and large the values in Table VIII support our general interpretation.

IV. DISCUSSION

The results of this analysis on the whole bear out the hypothesis which was being investigated. The canonical variate analysis gives results very similar to the factor analysis as far as the relative positions of individuals and diagnostic groups are concerned. It is found that on objective laboratory tests specially selected on the basis of a theory linking extraversion with high degrees of satiation and reactive inhibition, and introversion with low degrees of satiation and reactive inhibition, hysterics are discriminated from dysthymics with almost perfect precision while normal and psychotic individuals are intermediate between these two highly extraverted and highly introverted groups respectively. These results very much strengthen two aspects of the general theory under investigation. Namely, (1) the hypothesis linking extraversion and inhibition/satiation, and (2) the hypothesis linking extraversion with hysteria and introversion with dysthymia. It is very unlikely that factor analysis and canonical analysis of discriminance would have given results so much in agreement with each other if either one or both of these hypotheses had been seriously in error. It will also be noted that psychiatric diagnoses as used here could not be quite as unreliable as is sometimes suggested; extreme unreliability in the assignment of individuals to diagnostic groups would of necessity make the discovery of significant latent roots impossible. The reason, presumably, lies in our attempt to obtain subjects on whom there was considerable agreement among psychiatrists; the frequently observed unreliability of psychiatric diagnoses when random samples of patients are under investigation probably results from the large number of subjects whose position on the various continua involved is intermediate between those points singled out by the prevalent system of classification. This would appear to be but another argument in favour of the dimensional approach as opposed to the categorical diagnostic one.

V. SUMMARY

A battery of objective psychological tests, selected according to a specific theory of anxiety and hysteria, was administered to groups of hysterics, dysthymics, psychotics and normals, equated for age, sex and intelligence. The results were analysed by two different methods, (1) Multiple Factor Analysis, and (2) Canonical Analysis of Discriminance. The factor analysis disclosed, as expected, a strong factor of extraversion; factor scores estimated for this factor showed hysterics to be the most extraverted and dysthymics to be the most introverted of the groups tested. The canonical analysis of discriminance revealed two significant and one suggestive factor identified as extraversion, psychoticism and neuroticism. When individuals were given scores on the first two variates it was found that hysterics had the highest extraversion scores and dysthymics the highest introversion scores. Correlations between factor scores and variate scores show considerable agreement between the two methods in placing individuals along this dimension. It was concluded that the results supported two hypotheses. 1. Hysterics are characterized by a high degree of extraversion, while dysthymics are characterized by a high degree of introversion. 2. The theory according to which the tests were selected as measures of extraversion and introversion is supported by the results of the analyses, particularly by their congruence. It is suggested that canonical analysis of discriminance is a powerful and useful method in investigating dimensional problems of nosology and may have advantages in certain circumstances over the more widely used method of factor analysis.

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FIVE-YEAR FOLLOW-UP OF RESULTS OF RESERPINE THERAPY IN MENTAL HOSPITAL PRACTICE*

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Reserpine was first used extensively in mental hospital practice in this country in 1954. Conflicting reports as to its usefulness in psychiatry have appeared and, before a standardized assessment of the drug could be made, investigators examined the combined use of reserpine and chlorpromazine (Barsa and Kline, 3). Hare *et al.* (10) have pointed out that there is a sequence of events in the investigation of a new drug that is associated with a fluctuating enthusiasm as to its usefulness, and it is our belief that a commentary now on the present use of reserpine would not be out of place. Kline (13) was one of the first to describe the use of reserpine in American psychiatric practice, and his report was shortly followed in this country by those of Foote (8) and Glynn (9). These early studies were essentially preliminary investigations and concerned the use of reserpine in groups of patients, sometimes small, or of one sex. Other more extensive North American investigations by Noce *et al.* (17) and Azima *et al.* (2) showed that the beneficial effect of the drug was not as widespread as originally thought, even with adequate dosage, in schizophrenia. Barsa and Kline (4) produced further conflicting evidence that the drug was of value in all kinds of mental illness, although in a later paper in 1956 (3) they outlined the comparative uses of reserpine when contrasted with chlorpromazine.

Unfortunately, the trend of findings in this country does not materially clear the view, and thus it is found that reserpine is considered of little value in neurotics by Folkson and May (7), and yet in a similar series of a "blind" investigation Davies and Shepherd (5) found the reverse. In a like manner Ferguson (6) has also commented on the controversy that has arisen as to the value of reserpine in treating schizophrenia. Leibermann and Vaughan (14) found that reserpine resulted in improvement when used in schizophrenia, but they observed that in no case was the structure of the psychosis altered. Shepherd and Watt (19), on the other hand, did not consider reserpine at all favourably in the treatment of schizophrenia, whilst Moore (16) recommended that a prolonged trial of the drug should be made in intractable illnesses before leucotomy is undertaken.

Most of the studies mentioned have not included observations on patients for long follow-up periods, and where a double-blind technique is carefully followed in the model investigations, such as that described by Wing (23) it is clear that this is outside the scope of the investigation. Ferguson (6) has described the two-year outcome in a treatment group of 40 female psychoses.

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* Study carried out at Hellingly Hospital, Hailsham, Sussex.

In this series are described the results of treatment in a group of 180 patients (74 males and 106 females) and those that have done well have been followed up for periods varying from three to five years. Observations have been made upon both male and female out-patients and in-patients, and have covered its use in conditions varying from neurotic states to psychotic illnesses.

Like Moore (16) our attention was drawn to reserpine by an article that appeared in the lay press. The mother of a patient suffering from schizophrenia asked whether it would be possible for her son to have this "Indian herbal treatment", that she had read about in the *Readers' Digest*. Its use described here, therefore, started in this quite unorthodox way and from this small beginning it has been extended in varying dosage to all types of psychotic illness. All of the patients were known individually over a long enough period of time for their previous reactions to other kinds of treatment to be familiar and for the writers to be aware of the spontaneous variations that have occurred in each.

There were 74 males and 106 females (total 180). Eighteen (7 males and 11 females) were out-patients, the remainder (162) being in-patients. Only those who completed an adequate course of therapy have been included, and the patients who responded significantly to treatment have been followed up for periods of three to five years. As will be observed, this is a descriptive study rather than a "blind" trial of the drug, but it is questionable whether a trial can be really blind when side-effects can so easily be recognized. Shepherd and Watt (19) and Leibermann and Vaughan (14) have commented on their frequency. The patients in this series came from any ward in the hospital and consequently there is little chance that any special care and attention, linked perhaps with a particular environment, might have played any material part in the result of treatment.

Dosage

The investigation can be divided into two phases:

(*a*) For the first 40 patients the dosage of treatment was very cautiously applied and increased. Thus treatment was started at a level of 0·25 mg. t.d.s., increasing every three or four days by 0·25 mg., until a daily total of 1·5 mg. was achieved. At this stage, even continuing treatment for some two months, no lasting significant changes were observed.

Of these 40 patients 18 were suffering from neuroses, whilst the remainder (22) had a schizophrenic illness. In each case the maximum daily total was therefore 1·5 mg., and this was maintained for periods ranging from six to twelve weeks.

For reasons shown below treatment was continued with the schizophrenic illnesses in a dosage extended along the lines described in the second phase.

(*b*) High dose—sustained technique.

This has been used in all of the psychotic disorders and has consisted of a daily total of reserpine of 12 mg., given either by tablet or an equivalent sized injection thrice daily. Only those patients who have had at least six to eight weeks of this daily level have been included. In all, 162 patients constituted this group.

If at the end of the period of treatment improvement resulted, then a maintenance dose of 1 mg. t.d.s., was continued.

The diagnosis of the total series is as follows:

	Males	Females
Schizophrenia (illness active for more than a year) ..	31	80
Manic depressive psychoses	16	15
Neuroses	7	11
Other	20	—
	74	106

Our results have been assessed by the person in clinical charge, but agreed by the other. The categories used were as follows:

Much Improved. Patients who have improved to such an extent that they are considered either to have recovered from their illness or could be considered well enough for discharge from hospital or out-patient care.

Improved. Used where there has been more improvement than can be accounted for by the natural variations of the disease as known in the individual patient, but not amounting to the status "much improved".

Not Improved. To include those patients whose symptoms have remained static or increased during the period of observation.

The assessment was made at the end of the course of treatment and was based upon the behaviour of the patient as reported by the nursing staff and the clinical interview, which was carried out both before and after the course of therapy. If the patient relapsed during the period of follow-up, either within or without the hospital, then note has been made of this deterioration. Those patients who have been discharged from hospital have been followed up and reassessed, both on the evidence of clinical interview in the out-patients' department and with the knowledge gained from an up-to-date Social Worker's report. In this way a composite assessment has been possible. The long-standing patients with schizophrenia who were discharged from hospital have been seen at 3-monthly intervals in the out-patient clinic. Social workers have also paid visits to the home, or lodgings, at regular intervals.

FINDINGS

Low Dosage Schedule

	Much Improved		Improved		Not Improved	
Illness	M	F	M	F	M	F
Neuroses	—	—	1	4	6	7
Schizophrenia	—	—	1	2	4	15
	—	—	2	6	10	22

Total: 40

Side-Effects

	Neuroses		Schizophrenia	
Side-Effect	M	F	M	F
Nasal stuffiness	1	3	—	—
Giddiness	1	1	—	—

High Dosage Schedule

Illness	Much Improved M	Much Improved F	Improved M	Improved F	Not Improved M	Not Improved F
Schizophrenia	7	10	7	23	17	47
Manic depressive psychosis ..	–	—	7	7	9	8
Other	–	—	3	—	17	—
	7	10	17	30	43	55

Total: 162

Side-Effect	Males	Females
Drooling: Parkinsonism	24	40
Hypotensive phenomena	2	3
Nasal stuffiness	7	10

Of the 10 female patients who recovered, the most striking changes occurred in the long-standing, catatonic schizophrenic illnesses. The complete remission that took place in two of these patients was well beyond the natural variations of the disease. Formerly these patients had been homicidally aggressive, had spent many hours in seclusion and most of the time had been completely inaccessible; they showed so much nonsensical inco-ordination of thought processes that conversation was out of the question. All kinds of physical treatment had been tried without success (E.C.T., Cardiazol, coma insulin and standard pre-frontal leucotomy). Within six weeks of completing treatment with reserpine in adequate dose (4 mg. t.d.s.) both patients had become more composed and co-operative. The remission in both of these patients has been maintained and it has been possible for them to be discharged from hospital; they continue to support themselves in the community, coping with residential domestic tasks. What has been most striking is the sustained amnesia for events over the whole of their long stay in hospital (seven years and fifteen years respectively). Moreover, one of these patients has been able to discuss freely traumatic events that she says occurred before her admission.

SIDE-EFFECTS

Side-effects are troublesome during the acute phase of reserpine treatment and occurred in over 50 per cent. of the patients. The impression has been gained that this is very much an individual response and it bears no direct relationship to the dose. Some of the low dosage patients suffered side-effects even in daily totals of 1·5 mg. Cessation of the drug has always resulted in a disappearance of the phenomena. No epileptic fits occurred during the courses of treatment.

Unfortunately, one patient developed acute yellow atrophy and died. Post-mortem findings confirmed the clinical diagnosis. It has been impossible to demonstrate any direct relationship between this event and the giving of reserpine, and as far as can be ascertained from the literature, no previous incidence of this has been recorded. The patient had received a total of 12 mg. reserpine daily for a period of three weeks, but then became jaundiced. The drug was stopped immediately, but the icterus deepened and the patient died after having been in coma for three days. Stuppy and Tober (21) state that prolonged administration of reserpine in large doses to rabbits, monkeys and dogs did not result in any macroscopic or microscopic pathological findings in the heart, spleen, liver, kidneys, adrenals, stomach or intestine. The appearance of jaundice during reserpine therapy has not previously been described, and the possibility of the patient having recently had chloroform, amidopyrine or chlorpromazine was ruled out. It is difficult, therefore, to know whether there is any relationship at all between reserpine and hepatic damage.

Suicide

One patient committed suicide whilst undergoing treatment. She was suffering from a recurrent endogenous depression, had received two previous courses of E.C.T., with temporary benefit, and had refused more. Reserpine was tried in an attempt to remove the agitation and tension.

Maintenance Therapy and Relapse Rate

Whenever a therapeutic response to reserpine was obtained it was the aim to continue with therapy at a reduced maintenance level of 1 mg. b.d. This has not always been achieved, amd it has been found particularly difficult to know whether co-operation has been complete when patients have been discharged from hospital.

Of the patients who had "much improved", 5 males and 5 females have since relapsed, whilst of the "improved" category, 10 males and 8 females have deteriorated and thus reverted to their pre-treatment state. Eleven of the patients, from both of these categories, had been discharged from hospital and in each instance re-admission became necessary. The relapses have occurred within the first six months of the follow-up period and in only 2 of these patients has a resumption of high dosage resulted in a further improvement in condition. The exception to these observations was one patient whose reserpine was discontinued after three years in order to carry out serological investigations for a rare form of congenital jaundice. Within one week he became acutely hallucinated, suspicious and showed gross behaviour disturbance. A resumption of reserpine on completion of the biochemical investigations resulted in only a partial improvement, the thought disorder seeming to be uninfluenced.

The impression gained is that relapse can occur even whilst maintenance therapy is carried out, and in a certain number of patients resumption of reserpine in the initial higher dosage does not result in as good a response as on the first occasion.

Comparison of Dosage Techniques

The High Dosage and Low Dosage techniques have been described above and a comparison of the results of such treatment is as follows.

Of the 22 schizophrenic patients who had both Low and High dosage techniques, only 3 improved whilst on the smaller daily total, whilst 11 improved materially (4 males and 7 females) on the High Dosage technique. Although these are very small numbers the effect was sufficiently marked to continue the High Dosage method for the remainder of the series. The two most striking results were achieved in patients who had both small and large doses, and although both improved to a limited extent on 1·5 mg. per day, the subsequent change on 12 mg. per day was quite out of all proportion to that observed initially.

The Effects of Reserpine on Mentation

Kline has commented on two main phases in the development of the action of reserpine, a Sedative and a Turbulent phase. It has not been possible to confirm this clear demarcation, but the following comments upon the action of reserpine on schizophrenic thought processes can be made. Patients who are responding to the drug satisfactorily do not do so at the expense of the production of sleep or the mere slowing down of disordered thought processes, but rather by the emergence of a clear sensorium and a complete disappearance of schizophrenic thinking. Thus the reaction of reserpine is in complete contrast to the effect on mentation of, say, barbiturates.

This change takes place and is also associated with a return to normal of motor activity. It can be argued on this basis that whereas reserpine acts in schizophrenia it does not do so by producing the equivalent of a chemical leucotomy, but rather in resulting in a complete remission of active symptoms. It was found that in long-standing schizophrenic illnesses, i.e. those of over ten years' duration, although a remission of behaviour and thought disorder occurs, there still exists an emotional rigidity and flatness. This is presumably the aftermath of the psychotic process and is also observed in long-standing schizophrenic illnesses which are said to have "burnt themselves out".

If these observations on the selective action of reserpine on disordered thought processes can be confirmed, it might clarify part of the so-called "tranquillizing effect" of this drug.

Discussion

It is, of course, possible that there is no specific relationship between the remission of schizophrenic thought disorder and the administration of an adequate dosage of reserpine. It was, however, observed that in patients receiving the smaller dosage (i.e. 1·5 mg. per day) no improvement occurred and it was only on the exhibition of a higher dosage (i.e. 12–15 mg. per day), and even then only after some six to eight weeks, that remission occurred. Whilst these observations may have been biased, as this was not a "blind trial", it has been noticed that the remission occurred *pari passu* with the end of the course of adequate treatment.

Of the female patients suffering from long-standing schizophrenic illnesses, two have made remissions after nine and fifteen years respectively in hospital. In contrast, although some male patients showed improvement, none made a complete remission after such long periods of time. The numbers, of course, are far too small to regard the results as having any significance based upon the sex of the patient, but since both these female patients would otherwise probably still be in hospital, it follows that in this respect, the results of treatment were much more favourable with the female than with the male patients. It can, of course, be argued that this has only arisen by chance and, indeed, that the clinical changes that have been observed are linked with spontaneous remissions that can arise, even in schizophrenia. Mayer-Gross *et al.* (15) point out, however, that the prospect of a lasting, spontaneous remission after five years of continuous illness is negligible. Both the female patients mentioned remain out of hospital—five years afterwards—free from signs of active psychotic illness, and some explanation must be sought for these events. If one assumes, therefore, that the remission that has occurred has had some relationship with the exhibition of reserpine, one wonders if one is justified in taking the view that this is a specific action of reserpine on schizophrenic thought disorder. It is not considered that this can be claimed from the present findings and search must be made elsewhere for some explanation.

The patients in whom these marked improvements have occurred previously spent most of their days in seclusion in the "protected room". This reflected in a way the therapeutic milieu which then existed. It was based upon a time-honoured practice where the emphasis was upon seclusion rather than approaching refractory behaviour by active therapeutic means. The number of hours of seclusion in this hospital over recent years were as follows:

1953	12,110
1955	10,517
1957	1,078

As this study commenced in 1954, it will be seen that patients were moving in an environment where there was a preponderance of social isolation. Even with the advent of physical methods of treatment and reserpine we found that the attitude of ward sisters and charge nurses had to be overcome. This was natural in view of the aim of avoiding trouble at all costs. Gradually as the nursing staff realized that some significant change had taken place in the patients' condition it became possible for these patients to be allowed out of their room into the ward proper. These conditions have been described in detail, not because we feel that they were out of the ordinary at that time, but that they may have contributed to the changes that we have observed.

The most striking improvement occurred in patients who were spending most of their time in seclusion, i.e. their environment was very restricted. Reserpine, administered in adequate dosage, quickly brought the behaviour disturbance under control and although the termination of seclusion proceeded slowly, it ultimately resulted in an extension of the environment and a widening of the patient's horizons. In this way sensory deprivations have been overcome, and although the majority of the wards were still locked, it can be argued that sufficient impetus had been given to an extension of thinking, so that ultimate reintegration of perceptual processes occurred. Reserpine may in this way, by overcoming the behaviour disorder, allow perceptual processes to re-establish themselves.

This explanation precludes any specific action of reserpine on schizophrenic thought disorder. It is not possible to say how closely these observations tally with the so-called "break through" described by Kline (13), but the significance of them has already been mentioned by Azima *et al.* (2). Further studies centred on this problem seem desirable.

Further Commentary on Suicidal Preoccupation During Reserpine Therapy

The suicidal behaviour of one patient has been described and it is well recognized from other people's studies that severe depression can arise during the course of reserpine therapy, even although the dosage may be small. It seems difficult to prove from the present facts that the two states are necessarily linked. That depression should arise in people who have evidence of arteriosclerosis is not unexpected, particularly in view of the well-established relationship between the manic depressive psychosis and arteriosclerosis (Mayer-Gross, Slater and Roth, 15). It can be argued, therefore, that such depressive states that have arisen *de novo* may have occurred by chance and at the most, reserpine could only be considered as a precipitating factor. If the significance of the relationship between reserpine and suicide or depression is taken any further, then one presumes that this is a specific action, and would result in one being able to claim that a depressive psychosis could be produced by specific chemical means. In the present state of medical knowledge this claim does not seem justifiable. Ayd (1) also came to this conclusion.

DOSAGE

During the review of the literature on the use of reserpine in psychotic disorder, it soon became apparent that an adequate dosage is important. In the work of Swenson *et al.* (22) the daily total was at the most 4 mg., and the course of treatment consisted of some three months at this level. In like manner, Sommerness *et al.* (20) used a daily total of 3 mg., also continuing this for a period of three months, and they showed that reserpine had no effect upon psychotic behaviour. Penman and Dredge's work (18) showed that although they used up to 8 mg. per day over a period of three months, they were not satisfied that this dosage was adequate. Reserpine was not found at all helpful in dealing with neurotic illnesses, in fact considerable trouble was experienced with side-effects and Davies and Shepherd (5) appear to have had similar results. On the other hand, once it had been established what constituted an adequate dosage in dealing with psychotic behaviour, reserpine was found of value in dealing with schizophrenic illnesses. Hoch (12) states that 5 per cent. of chronic schizophrenic conditions will improve, and in this trial it was found that the most significant improvements occurred in patients in whom the illness had existed for more than ten years, had previously given a negative response to other kinds of treatment given, and often associated with the most severe behaviour disorder and disturbance of thought processes. It is, perhaps, this kind of case that Azima *et al.* (2) had in mind when they noted changes in schizophrenics, although unable to find any distinctive clinical characteristics. It can be argued that the progress made by even one of these patients is worthwhile and that it does not necessarily follow that Hollister's claim (11) in which chronicity was linked with poor prognosis is correct. From the point of view of behaviour, there is a certain amount of evidence to show that the greater the behaviour disturbance the more likely reserpine is to help.

SUMMARY

1. The use of reserpine in mental hospital practice has been described.

2. It is considered that an adequate dosage is somewhere between 8 and 15 mg. per day, continued over a period of six to eight weeks.

3. The drug is of most value where there is marked psychotic behaviour present and extraordinary changes can occur in schizophrenia. Maintenance therapy is desirable.

4. Side-effects in psychotic patients are reversible and do not present a very great practical problem.

5. Results of treatment in neurotic illness with reserpine have been most disappointing, as has also been the use of the drug in depression.

6. One instance of acute yellow atrophy during reserpine therapy is described.

7. Attention is directed towards the action of the drug upon thought disorder. Suggestions are made as to its possible method of action.

ACKNOWLEDGMENTS

Our grateful thanks are due to our colleagues and members of the nursing staff for their interest and co-operation in this work. Throughout this trial "Serpasil" brand of reserpine was used, and we would like to acknowledge our debt to Messrs. Ciba Ltd., who supplied this free of charge, and to their Medical Director, R. K. Pitman, for his personal interest and help.

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ASPECTS OF EXTRA- AND INTRO-PUNITIVE EXPRESSION IN MENTAL ILLNESS

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INTRODUCTION

THE terms *extrapunitive* and *intropunitive* were introduced by Rosenzweig (1938) to denote two of the possible ways in which an individual might react to frustration or blame. He defined the extrapunitive reaction as: "When the individual tends to blame the external world, reacts with anger and hostility, and psychologically defends himself by what the psycho-analyst describes as the mechanism of projection. An ego which fears blaming itself thus gains security by blaming others instead".

The intropunitive reaction he defined as: "When the individual tends to blame himself, reacts with feelings of remorse and guilt and employs the mechanisms of defence called by the analyst displacement, isolation and undoing. An ego which fears blaming others thus gains security by blaming itself instead".

Whilst he recognized that no individual would react consistently in one particular way, he did envisage that certain types of individual might be characterized by a disposition to act more frequently in one way rather than in another. He did, for example, speculate that Paranoid patients might show a preference for extrapunitive responses; whilst Obsessional patients might show a preference for intropunitive responses. Many clinicians would like to add psychotic depressives to the intropunitive side.

Rosenzweig's original linkage of his terms with psycho-analytic concepts was perhaps unfortunate. Had the terms extrapunitive and intropunitive simply meant directing blame outwards and inwards respectively, the examples given by Rosenzweig would more readily have been seen as special instances of these main types of reaction. The psycho-analytic propensity for generalizing from atypical particulars too easily results in adoption of the view that anger and hostility *always* arise in a setting in which the ego fears blaming itself. This over-emphasis on intra-psychic determinism may give rise to the view that any form of criticism of others is fundamentally of a paranoid nature.

An investigation by Brown and Lacey (1954) illustrates the confusion likely to arise from associating extrapunitiveness exclusively with psycho-analytic projection and hence with paranoia. These authors using a projective test—Rosenzweig's Picture-Frustration Study—failed to find the relationship between extrapunitiveness and paranoid states. Examination of the items in the PF study would not, however, lead one to expect such a relationship, since the extrapunitive responses might include acting-out hostility, verbal criticism of others or projected hostility in the psycho-analytic sense. Thus, one picture shows a man being splashed by a passing car, in which are two other men. The reaction might be to hurl at the driver a brick (acting-out) or abuse (criticism of others) or to do and say nothing, but go away confirmed in the belief that the International Gang was still out to get him, because they knew that he could expose them to all the world and put right the wrong that had been done to him (projected hostility). It is only in respect of this last type of response that one would confidently predict the association with paranoid patients.

Similar difficulties would present themselves over intropunitiveness and psychotic depression (henceforth, for brevity, and to sharpen the distinction from psychoneurotic depression, referred to as Melancholia). The pedestrian might reply: "Don't worry, it was my fault. I wasn't looking where I was going" (self criticism) or he might go on his way thinking "people revile me and cast mud at me, because I am a wicked sinner" (guilt). It is only with the second type of response that one would confidently associate Melancholia.

That not all psychiatrists would agree in associating projective hostility so specifically with paranoid states has been brought out by Lewis (1934). The following citations, taken from the survey by Lewis and ranging from 1892 to 1934, probably illustrate current views with fair accuracy:

Thus Stoddart (1919) apparently recognizes that paranoid delusions may be part of the melancholic picture: "There is another class of melancholics . . . who . . . develop delusions of persecution, they believe that other people are against them, even that there are world-wide conspiracies to do them harm."

The next three authors, however, make a firm distinction between extrapunitive and intropunitive delusions. Séglas (1892): "The persecutory ideas found in deluded melancholics are not true ideas of persecution. Their foundation is not pride, but the peculiar humility of the melancholic; they bear the stamp of that peculiar quality of resignation which is their own; for the patient finds his persecution justified by his unworthiness, and, notwithstanding the 'persecution' label we attach to his delusions, he remains first and foremost a self-accuser."

Ballet (1892): "They are victims, but guilty victims, not as ordinary patients, innocent victims."

Bleuler (1924): "Delusions of persecution do not belong to the depressive forms of delusion. The delusion of deserved punishment must not be classed with that of the unjust persecution."

Lewis (1934) takes up an intermediate position: ". . . humility and resignation are by no means the only attitude the melancholic patient takes up, but . . . resentment and hostility may exist alongside these, or may even dominate the picture. . . . Resignation is certainly the commonest attitude towards the persecutory ideas, but it is not by any means the invariable one. It may be said that it is an admixture of other forms or reaction-types, which produces in some patients a resentful attitude towards the supposed discrimination, but where so small a number out of 61 patients are quite free from such features, one is more inclined to regard it as part of the depressive type of reaction."

The terms *extrapunitive* and *intropunitive*, in the wider sense suggested above, are tolerably accurate descriptions of the contrasting attitudes discussed by these psychiatrists. Despite the shrewdness with which these observers disentangled these attitudes, they nevertheless sometimes arrived at different conclusions. Séglas, Ballet and Bleuler reject extrapunitive delusions in Melancholia; Stoddart accepts the opposite view and Lewis takes up an intermediate position. The present investigation provides some information relevant to this divergence of opinion.

In a recent study (Foulds and Caine, 1959a) of which this is an extension, two scales constructed from the Minnesota Multiphasic Personality Inventory to measure the different aspects of intropunitiveness referred to above (viz. self-criticism and guilt) were described. These scales were found to function differently from each other when applied to psychoneurotic and psychotic groups. Siegel *et al.* (1957) have reported what they described as three hostility sub-scales (of the questionnaire type) measuring extrapunitiveness, intropunitiveness and projected hostility; but these terms were used somewhat differently.

Caine (1959) has described two measures (one questionnaire, one projective type) which could be said to represent acting-out hostility, projected hostility and undifferentiated self-criticism and guilt. These measures showed differences in the expected direction between melancholic and paranoid women. Acting-out hostility failed to differentiate; but projected hostility and self-criticism/guilt both differentiated at a high level of statistical significance. Foulds and Caine (1958, 1959b) have found that undifferentiated scales of extrapunitiveness and intropunitiveness were related to personality types rather than to diagnosis in neurotic men and women.

Although there is some overlap of subjects in three of the studies mentioned, they do lend support to the clinical view that mentally ill persons express their extrapunitiveness and intropunitiveness in characteristic ways. Despite the long history of these observations, just what is implied by these terms is still far from clear.

The main purpose of the present study then, is to justify breaking down the extrapunitive and intropunitive M.M.P.I. scales into five sub-scales. In furtherance of this aim it is necessary:

1. To see how far such a breakdown can contribute to our understanding of the attitudes to *self* and to *others* of various clinical groups;

2. To exploit for diagnostic purposes such between-group differences as might be found; and

3. To seek to understand the relationships between these sub-scales by means of within-group correlations between scales.

In the sections on procedure and results these three related problems are treated separately.

PROCEDURE

1. *Attitude to Self and Others*

The *extrapunitive scale* was broken down into three sub-scales on the basis of the following arguments. From clinical and experimental evidence there are three characteristically extrapunitive groups, namely psychopaths, paranoids and, in women, hysteroid personalities. These three groups will, it was predicted, express their hostility in different ways. The distinguishing feature of the psychopath, in relation to the other groups, will be the *acting-out* of his aggression readily admitted and defended. Although aggression may be ascribed to others as well, it will not be denied in himself. On the other hand acting-out hostility will be denied by the paranoid who will project it on to others. Thus the paranoid will feel himself in receipt of *a direct, personal attack from others to a degree such that the question of delusional thinking might well be raised.* In contradistinction to these two groups, hysteroid women will have neither of these predispositions to a marked degree. *Vis-à-vis* female obsessoid personalities, hysteroids will be generally more *critical of others* in attitude, without feeling personally attacked or required to attack others.

In selecting items from the M.M.P.I. (see Appendix A) for these three extrapunitive sub-scales of Acting-out Hostility (AH), Projected Delusional Hostility (DH) and Criticism of Others (CO), it was found that the AH scale presented the least difficulty. This consisted of relatively unambiguous items, such as (G-31) "At times I feel like smashing things" and (G-32) "At times I feel like picking a fist fight with someone".

In selecting items for the DH scale, to differentiate it from the merely critical attitude, an attempt was made to choose only those items in which a direct, personal receipt of hostility from others was implied, an act of open enmity about which the question of delusional thinking might well be raised. Thus (H-4) "I believe I am being followed", or (H-11) "I believe I am being plotted against".

The CO scale, unfortunately, tended to be somewhat more ambiguous since many of the M.M.P.I. statements might include, in addition to criticism of others, an implication of acting-out or of projection: for example (C-31) "I have at times stood in the way of people who were trying to do something, not because it amounted to much but because of the principle of the thing", although not implying violent physical assault, does suggest action being taken. Most of the remaining items included in this scale were either criticism of others only, or criticism of others with projection. Thus (C-3) "Some of my family have habits that bother and annoy me very much", may be criticism of others if the respondent either has not got, or does not deny, these habits in himself. It may, on the other hand, include a projective element if a majority of competent observers consider that he, rather than members of his family, has the tiresome habits. The projective element, in such an instance, though self-deceptive, would not generally be regarded as necessarily psychotic. Neither is a deliberate, active attack implied. To this extent it should be noted, there is some unavoidable, if regrettable, overlap in the sub-scales.

With regard to the *intropunitive scale* the sub-scales previously described (Foulds and Caine, 1959a) have been applied to this wider range of clinical groups. It was argued that Melancholics, *vis-à-vis* other groups, would be the high scorers on the Guilt scale (DG). This scale consisted of items involving *the perpetration of actual harm on others with accompanying guilt or deserved destruction of the self by disease or by others. The question of delusional thinking might again be raised*, as, for example, in (F-50) "Much of the time I feel as if I have done something wrong or evil". On the other hand, the other known intropunitive group, the obsessoid male neurotic, would be distinguished from the melancholic by his absence of guilt, but from the other groups by his high score on the Self-Criticism scale (SC). As distinct from the DG scale which involves the perpetration of harm on others, this SC scale consists of items *questioning one's own ability and adequacy in particular areas*, such as (A-23) "I (do not) seem to be as capable and smart as most others around me", or (I-41) "I shrink from facing a crisis or difficulty".

In addition to these specific predictions of high scoring, certain low scoring was also anticipated. Paranoids, if (as Rosenzweig claims) projection occurs "when the ego fears blaming itself" should have low SC scores. They should also have low AH scores, since they deny hostility in themselves and project it on to others.

The Psychopathic lack of conscience and of any standards to which one can appeal should ensure a low SC score. Melancholics, being, in the psychoanalytic view, afraid of blaming others, gain security by blaming themselves instead. They will, therefore, score low on CO.

In previous investigations (Foulds and Caine, 1958; Foulds, 1959) obsessoid Dysthymic women scored lower than hysteroid Hysterics and Dysthymics on the undifferentiated extrapunitive scale. Since there seems no reason for them to differ on the "psychotic" DH scale, obsessoid Dysthymic women will probably score significantly lower on AH and CO.

2. *Diagnostic Purpose* (*Between-group Differences*)

It was not considered likely that one combination of the five scores on the sub-scales, however weighted, would stretch out all the diagnostic groups along one continuum. The most appropriate method seemed to be to take each diagnostic pair in turn and, by means of the discriminant function technique, give suitable weights to the measures which helped to distinguish between the two groups concerned. This method has, of course, some limitations; but in clinical work, they are apt not to be too serious. The great majority of diagnostic problems only involve two possibilities. Even if the psychologist were starting from *carte blanche*, the pairing method might still be feasible. Measures might be used which were known to differentiate say, psychotics from neurotics. If the answer suggested odds on neurosis, one might then proceed to measures known to differentiate Hysterics from Dysthymics. If the answer this time suggested Dysthymia, one might then proceed to measures known to differentiate Anxiety States from neurotic Depressives and Obsessionals.

3. *Relationship Between the Sub-scales*

Correlations were calculated for all scales within each group. It was anticipated with regard to the relationships between the sub-scales that the within-group correlations between the three extrapunitive and between the two intropunitive sub-scales would be substantially higher than between any extrapunitive sub-scale and any intropunitive sub-scale. If Rosenzweig is right with regard to projection and self-blame, DH and SC should be negatively correlated.

SUBJECTS

Cases were randomly selected from the files until groups of 20 men and 20 women had been completed for each of the following categories (with the exception of Psychopathic women, of whom only 11 were available): Hysterics of hysteroid personality (Hh); Dysthymics of hysteroid personality (Dh); Dysthymics of obsessoid personality (Do); Melancholics (M); Paranoid States (PS) and Psychopaths (Pp).

It was later ascertained that 75 per cent. of these cases had been used in previous research projects. These cases were successive admissions constituting an unselected population at the time of testing. The remaining 25 per cent. were referred by the psychiatrists for a clinical opinion and might, therefore, be presumed, in the majority of cases, to be less typical of the nosological groups to which they were ultimately assigned. The proportions of these two types of cases were fairly evenly distributed among groups, except that the male melancholics and both psychopathic groups were somewhat overloaded with clinical referrals. There was, however, no contamination of test results and clinical diagnosis in these cases, as the scales used here had not been devised at the time of testing and reporting.

The results obtained from 20 male and 20 female members of the hospital staff (or members of their families) were included for comparative purposes. There was some representation from each occupational group within the hospital.

RESULTS

1. *Attitude to Self and Others* (*Between-group Comparisons*)

The means for the seven groups are shown graphically for each measure and for men and women in Figure 1. An analysis of variance was carried out on each measure separately to see if differences between the means were significant and in Appendix B the means, standard deviations, standard errors of differences between means and F values are given. Means and standard deviations have been pooled where they did not differ significantly from one another. It can be seen that differences between women are more highly significant than those between men. A similar result was obtained in a recent study with neurotics (Foulds and Caine, 1959b). The pattern of results for men and women is, however, fairly similar for each of the variables. On *Acting-out Hostility*, Psychopaths were significantly higher than the rest for both men and women. The other groups did not differ significantly from each other, although for women obsessoid Dysthymics were almost significantly lower.

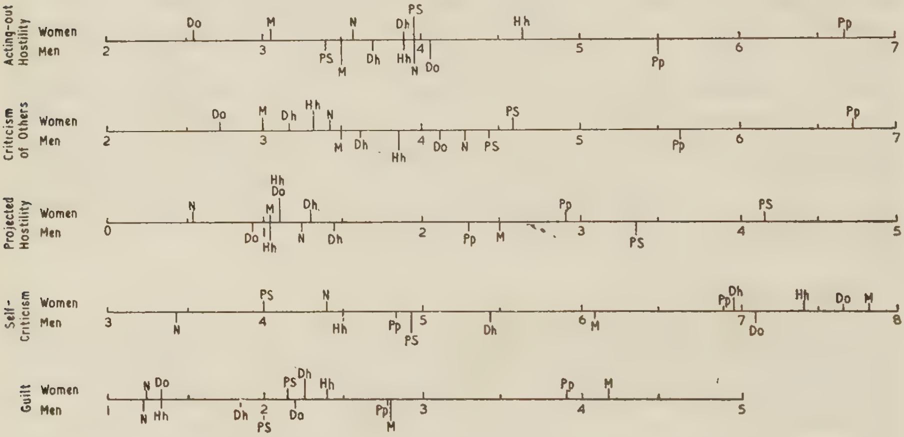

FIG. 1

On *Criticism of Others*, Psychopaths again had values significantly higher than the rest. For both sexes Paranoid States came next. For men, Paranoid States were very close to the other groups; but, for women, they were also significantly higher than the rest.

On *Projected Delusional Hostility*, variation between groups was more highly significant than for any of the others. In men, Paranoid States were highest and, taken together with Melancholics and Psychopaths, differed significantly from the other groups. For women, Paranoid States were again highest, followed by Psychopaths, and these two differed significantly from the rest.

On *Self-Criticism*, obsessoid Dysthymic men were significantly higher than the rest. Normals were significantly lower. For women, on the other hand, the only significant differences were caused by Normals and Paranoid States being significantly low.

On *Delusional Guilt*, the scores for men fell into three groups (which differed significantly), Psychopaths and Melancholics being highest, then obsessoid Dysthymics, Paranoid States and hysteroid Dysthymics, and lowest Normals and hysteroid Hysterics. In women the same two groups were highest; but the lowest two were obsessoid Dysthymics and Normals.

In general, it is quite clear that the sex differences are very much less prominent than the similarities.

Tables I and II show the predicted and observed outstanding characteristics of each clinical group among women and men respectively. From these tables it can be seen that the clinical groups revealed the characteristics which everyone would expect them to reveal, with perhaps three main exceptions—the high DH of male melancholics and the high DH and, above all, the high DG of both male and female psychopaths.

TABLE I

Showing the Predicted and Observed Outstanding Characteristics of Each Diagnostic Group (Women)

Predicted		Group	Observed	
High	Low		High	Low
AH	SC	Pp	AH, CO DH, DG	
DH	AH, SC	PS	CO, DH	SC
DG	CO	M	DG	
		Hh		
		Dh		
	AH, CO	Do		DG

TABLE II

Showing the Predicted and Observed Outstanding Characteristics of Each Diagnostic Group (Men)

Predicted		Group	Observed	
High	Low		High	Low
AH	SC	Pp	AH, CO, DH, DG	
DH	AH, SC	PS	DH	
DG	CO	M	DG, DH	
		Hh		DG
		Dh		
SC		Do	SC	

2. *Diagnostic Purpose (Between-group Differences)*

The best discriminant function to use to compare two groups is shown in Appendix C. The scales shown do not necessarily include only the measures for which the two groups differed significantly since the correlations between the measures affect the final result. Apart from hysteroid Dysthymics and hysteroid Hysterics, who had virtually the same responses, the discriminant function was always significant at the 1 per cent. level of significance, and frequently at the ·1 per cent. level. What this means in terms of prediction can be seen from the table. Amongst the women there was very little overlap between any two groups when the "best" measure was used to discriminate between them. For the men discrimination was not quite so good.

It has been shown previously (Foulds and Caine, 1958, 1959b) that Hysterics can be distinguished from Dysthymics, of no matter what personality type, by the M.M.P.I. Depression minus the Hypochondriasis (K corrected) scales for women and the Depression plus Psychasthenia (K corrected) scales for men. With a very considerably curtailed M.M.P.I. (containing only 168 items) it is, therefore, possible to differentiate with a useful degree of accuracy between as many as six different diagnostic categories for both men and women.

3. *Relationships Between the Sub-scales* (*Within-group Correlations*)

In Table III are given the correlations between the five variables taken in pairs, for men and women separately. These were calculated for variations *within* each group. They do not refer to the overall pattern of results, but to whether people within one diagnostic group tend to obtain similar scores. The various groups had correlations which were fairly similar and these have been pooled to give final values.

TABLE III

Correlations (*Average Within Groups*)

	Men					Women			
	C	P	G	S		C	P	G	S
A	·50	·31	·42	·35	A	·42	·41	·19	·21
C		·30	·13	·16	C		·43	·19	·18
P			·46	·36	P			·22	·16
G				·53	G				·59

All the correlations are positive. People scoring highly on one measure tend to score highly on the others, relative to other people in the group and vice versa. The prediction that DH and SC would be negatively correlated was not, therefore, confirmed. The DH:SC average within-group correlations were, in fact +·36 for men and +·16 for women. Amongst women, however, Paranoid States did score highest of all groups on DH and lowest of all groups on SC. Male Paranoid States scored highest of all groups on DH, but at an intermediate position on SC.

These results could perhaps be interpreted as indicating a "general hostility factor". The correlations between the three extrapunitive measures are, however, higher, on the average, than their correlations with the two intropunitive measures and the correlations between SC and DG is higher than all the others. This confirms the hypothesis that the extrapunitive scores are to some extent measuring something different from the intropunitive. This is clearer for women than for men. For men there are correlations of about ·4 between AH and DH and the two intropunitive scores (the corresponding values for women being about ·2). This problem of the factors has already been discussed elsewhere (Creasy, 1959).

Discussion

None of the within-group correlations between the scales is high enough to make any one of them superfluous. Each has, in fact, been shown to have been extremely effective in contributing to the differentiation between a wide variety of clinical conditions. In other words, each sub-scale appears to be measuring something sufficiently different from every other one to justify its separate existence. From the consonance of the scores with rather obvious clinical predictions, it would seem likely that these sub-scales are, in fact, measuring something approximating what they purport to be measuring. The most notable exception is provided by the Psychopaths. Either they are much more intropunitive than has usually been believed or they treat the test differently from the other groups. Some support is lent to the second view by the fact that, whilst they have scored very highly on both "psychotic" scales, the one scale on which they are second lowest of the clinical groups is SC. It would seem that Psychopaths may regard themselves as hot-tempered, cynical, interestingly mad or diabolically wicked; but that they draw the line at appearing faintly inferior or incompetent.

The principal remaining anomaly is the high DH of Melancholic men. One of the points at which the present study impinges most directly on significant clinical problems is in the differentiation between Melancholia and Paranoid States or Paraphrenia. Unfortunately, the question of whether ideas of persecution are felt to be justifiable or unjustifiable is ignored by the M.M.P.I. items. No direct evidence can, therefore, be offered. As has been noted, however, Paranoid women scored highest of all groups on Projected Delusional Hostility and lowest on Self-Criticism. Paranoid men scored highest on Projected Delusional Hostility, but at an intermediate position on Self-Criticism. Melancholic women scored lowest of all the patient groups on Projected Delusional Hostility; whilst Melancholic men scored second highest. This suggestive evidence raises the possibility that "justifiable" ideas of persecution may be commoner amongst men than amongst women. In other words, the position of Séglas, Ballet and Bleuler may be more applicable to Melancholic women than to Melancholic men.

G. W. Allport (1937) suggests that the mature personality is characterized by consistency and predictability of attitudes. From the present data it would seem unlikely that the converse holds. Psychoneurotics and, *mutatis mutandis*, psychotics, or at least psychotic depressives and well-preserved paranoid states, may well be extremely predictable in the areas studied here. Hilgard (1954) has pointed out that it is the integrative, not the integrated personality "which can handle the complexity of relationships with other persons in a culture like ours, a culture which makes plural demands. An integrated personality soon leads to its own isolation or destruction if it is not also integrative . . . the paranoid psychotic with highly systematized delusions is among the best integrated of personalities." If paranoids deny impulses or attitudes in themselves, which they then attribute to others, they cannot be among the best integrated of personalities in the sense of wholeness or one-ness. They only achieve a pseudo-integration. This perhaps becomes more apparent when grandiosity rather than persecution dominates the picture, as, for example, in the patient who believed that she was a Duchess, but was quite content to do menial work in the hospital without any apparent awareness of incongruity. Nevertheless, it is often said that given the initial premise everything else follows logically in paranoia. It would perhaps be truer to say that everything else follows rather predictably, since the basic delusion acts as a vortex swallowing up everything within the field. These patients may be thought of as less stimulus-bound than the normal person, since the main function of their defensive attitudes is to maintain, by constantly reinforcing the basic delusional belief, what integrity of personality is left to them, even to the extent of highly idiosyncratic selection and, indeed, gross distortion of external stimuli.

One of the inadequacies of the present study is the fact that neurotics have been rated on a hysteroid:obsessoid personality scale; whereas psychotics have not. Amongst neurotics it was, in fact, found that the measures were related to personality type rather than to diagnostic type. It would be of interest to classify psychotics according to both types of category. It may be that in the psychoses, which are considered to involve more far-reaching disturbances of personality, the influence of the pre-morbid personality may no longer be apparent. One could, indeed, conceive of a continuum of influence of pre-morbid personality—at its greatest, amongst the mentally ill, in neurotics and lessening through Melancholia, Paranoid States, Catatonic Schizophrenia to Hebephrenic Schizophrenia.

However this may be, it would seem that, if these results can be replicated by other workers, these attitudes may prove to be rather central issues either in psychiatric illness or, at least, in the psychiatrist's clinical appraisal of his cases for diagnostic purposes. It may be argued that these attitudes are relatively accessible to observation, that they have in consequence been given great weight by psychiatrists and that all that these measures have done is to confirm this fact. When such confirmation reaches a level at which subjective and objective assessments become justifiably interchangeable, a considerable advance has been made. Aside from this, however, the speculation that a person's concept of himself and of others may be a matter of rather crucial concern to him is no longer universally condemned. It may not be unreasonable to assume that radical threats to these concepts would require drastic defensive measures against intolerable distress. In the main, it would appear that these drastic defensive measures succeed only in reducing intolerable distress to just tolerable distress for the person himself or intolerable distress for those with whom he is concerned. It is idle to suppose that any discipline which deals with less than the higher level functions in terms of less than the higher level functions, can provide any information which will reduce this deep concern of the individual with himself and his relationship to his fellows to an insignificant epiphenomenon.

SUMMARY AND CONCLUSIONS

Five scales have been made up from the Minnesota Multiphasic Personality Inventory. Three of these scales are concerned with aspects of extrapunitiveness–Acting-out Hostility; Criticism of Others and Projected Hostility. The remaining two are concerned with aspects of intropunitiveness–Self-Criticism and Guilt.

These five scales have been given to 20 women and 20 men in each of the following categories: Normals;—Hysterics of hysteroid personality; Dysthymics of hysteroid personality; Dysthymics of obsessoid personality; Melancholics and Paranoid States (including Paranoid Schizophrenics) and to 20 male Psychopaths and 11 female Psychopaths.

Within-group correlations between scales were all positive; but, when the size and pattern of the correlations were considered, it was clear that the extrapunitive scores were to some extent measuring something different from the intropunitive scores.

The discriminant function technique was applied to the differentiation between each possible diagnostic pair. It was found that, with the exception of hysteroid Hysterics and hysteroid Dysthymics, the discriminant function was significant at the ·1 per cent. level and frequently at the 0·1 per cent. level of significance.

Sex differences were found; but these were less marked than the similarities.

Amongst men, Psychopaths scored significantly higher on Acting-out Hostility and on Criticism of Others. On Projected Delusional Hostility their scores were exceeded (though not significantly) by Melancholics and particularly by Paranoid States. These three groups differed significantly from the neurotics and normals. On Self-Criticism, obsessoid Dysthymics scored significantly higher than all other groups and Normals significantly lower. On the Delusional Guilt scale, Psychopaths and Melancholics scored significantly higher than all others and Hysterics and Normals significantly lower.

Amongst women, Psychopaths scored significantly higher than all other groups on Acting-out Hostility and Criticism of Others. On Projected Delusional Hostility, their score was exceeded by the Paranoid States; but both of these groups were significantly higher than the remainder. On Self-Criticism, Paranoid States and Normals scored significantly lower than the rest. On the Delusional Guilt scale, Melancholics and Psychopaths were the highest and Normals and obsessoid Dysthymics the lowest.

Apart particularly from the high Delusional Guilt scores of Psychopaths, the clinical groups behaved as predicted (although differences which had been predicted were not always statistically significant). It was suggested that Psychopaths preferred to be thought wicked rather than incompetent.

Each of the five scales has contributed very considerably to differentiation between groups. The breaking down of the original extrapunitive and intropunitive scales was, therefore, justified. Indeed, the efficiency of these measures, if confirmed elsewhere, suggests that what a person reports about himself and others, in areas which may be broadly subsumed under Rosenzweig's headings of extra- and intro-punitiveness, may be of central importance to our understanding of the mentally ill.

ACKNOWLEDGMENTS

The authors wish to acknowledge their indebtedness to Dr. R. Ström-Olsen for permission to publish and for making it possible for the investigation to be carried out.

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APPENDIX A

The items from the abridged M.M.P.I. were as follows:—

AH: D-30, E-7, F-31, G-29, G-31, G-32, G-47, G-48, I-1, I-2, I-4, I-26, J-43.
CO: B-55, C-3, C-31, D-47, D-49, D-50, D-52, D-53, E-9, E-53, F-30, G-50.
DH: G-52, G-53, G-54, G-55, H-4, H-10, H-11, H-15, H-26.
SC: A-23, C-25, C-29, F-33, I-13, I-25, I-26, I-31, I-39, I-40, I-41.
DG: F-50, G-3, G-4, G-9, I-17, I-36, I-37.

APPENDIX B

Table Showing Means, Standard Deviations, Standard Errors of Difference and F Values

Women

	AH		CO			DH			SC		DG		
	Pp	Rest	Pp	PS	Rest	Pp	PS	Rest	N,PS	Rest	N,Do	Dh, Hh,PS	Pp,M
Mean	6·6	3·6	6·7	4·6	3·2	2·9	4·2	1·0	4·2	7·4	1·3	2·3	4·1
S.D.	2·9	1·9	2·6		1·9	2·5		1·0	2·5			1·6	
S.E.		·7	1·0		·6	1·0		·6	·3			·3	·3
F		5·1		5·8			11·7		7·8			8·6	

Men

	Pp	Rest	Pp	Rest	PS, M,Pp	Rest	N	Rest	Do	N,Hh	Do, Dh,PS	M,Pp
Mean	5·5	3·8	5·6	4·0	2·7	1·2	3·4	5·2	7·1	1·3	2·0	2·8
S.D.	3·4	2·2	2·6		2·4	1·3		2·7			1·5	
S.E.		·8		·6		·3	·7		·7		·3	·3
F		1·7	1·5			6·7	3·7				3·5	

Significant values of F: ·05=2·2, ·01=3·0, ·001=4·0

APPENDIX C

A discriminant function has been calculated for each of the pairs of groups, hysteroid Hysterics and hysteroid Dysthymics being taken together. These are given below and have been adjusted so that a negative score means allot to one group and a positive score allot to the other. The percentages in the observed groups having these scores are given and the significance of the discrimination. These are the appropriate criteria if initially there is a 50:50 chance of a person coming from one or other of the groups.

Women

	PS	Do	PS	M	PS	Pp	PS	Dh,Hh	Do	M
<0	10	100	10	100	90	27·3	15	92·5	95	20
>0	90	0	90	0	10	72·7	85	7·5	5	80
	AH+4DH+3DG −3SC−0·5		3DH−DG−SC +0·5		3AH−5DH+2DG +SC−15·5		−AH+4DH+DG −SC−2·5		3DG−SC−1·5	

	Pp	Do	Do	Dh,Hh	M	Pp	Dh,Hh	M	Dh,Hh	Pp
<0	9	90	35	80	90	0	77·5	25	97·5	18·2
>0	91	10	65	20	10	100	22·5	75	2·5	81·8
	AH+CO+3DG −2SC−3·5		2SC−2DG−AH −8·5		2AH+2CO−SC −9·5		3DG−AH−5·5		CO+DG−9·5	

Men

	PS	Do	PS	M	PS	Pp	PS	Dh,Hh	Do	M
<0	20	95	35	65	70	40	20	77·5	70	25
>0	80	5	65	35	30	60	80	22·5	30	75
	3DH−DG−SC +0·5		DH−DG−0·5		AH+2CO−5DH +3DG−7·5		DH−1·5		3DH−SC+1·5	

	Do	Pp	Do	Dh,Hh	M	Pp	Dh,Hh	M	Dh,Hh	Pp
<0	65	30	55	85	85	40	70	40	67·5	30
>0	35	70	45	15	15	60	30	60	32·5	70
	2CO+4DG −SC−2·5		SC−DH−6·5		2CO−SC−4·5		DH+DG−3·5		3CO+5DG −2SC−15·5	

PHOTOCONVULSIVE THRESHOLD IN DEPRESSIVE ILLNESS AND THE EFFECT OF E.C.T.

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FEW techniques are available which have as their aim the quantitative determination of a physiological function of the human brain. Of these the photomyoclonic threshold has received most attention and numerous reports have appeared concerning findings in epilepsy, schizophrenia, other psychiatric conditions and normal controls (2, 4, 5, 9, 10, 11, 14). The precise neurophysiological meaning of the "threshold" is unknown but since the first publications of Gastaut (5) it has been widely assumed that the measure is one of diencephalic function and that a change in the latter can be detected by the resulting threshold change.

The present study is concerned with the photo-convulsive threshold in a group of patients with depressive illness before and after electro-convulsive therapy (E.C.T.). Previously published work on the effects of E.C.T. in this respect has been limited to the study of very few cases (10) or has made use of a different index of "threshold" (3).

MATERIAL AND METHODS

Twenty-seven adults (Table I) diagnosed by the consultant psychiatrist in charge as having a severe depressive illness and admitted to the Maudsley Hospital as in-patients were the subject of the investigation. Of the 18 who had had successful determinations of threshold before and after E.C.T., 7 expressed suicidal ideas and 11 had had previous depressive episodes.

Each patient had an EEG before any further investigation or therapy, a brief "resting" record being followed by successive periods of hyperventilation and photic stimulation.

The technique of measurement of photomyoclonic threshold was a modification of that of Ulett *et al.* (16), 0·5 ml. 1 per cent. hexazole (Azozol, Boots) being injected rapidly into an ante-cubital vein every 30 seconds, each injection being followed after 15 seconds by a 15-second period during which photic stimulation (electronic stroboscope 8 cm. from the closed eyes in a darkened room) at 18 flashes per second was given. The cycle of injection, pause, photic stimulation was repeated at 30-second intervals until spike-and-wave or multiple spikes appeared in the EEG, or myoclonus extending beyond the face was seen in the patient. The threshold so obtained was taken to be the total amount of hexazole in milligrams injected up to the appearance of the end-point

TABLE I

(1) No.	(2) Age	(3) Sex	(4) Weight Kg.	(5) T_1 mg.	(6) T_2 mg.	(7) No. of E.C.T.	(8) Interval Days	(9) Post-E.C.T. EEG	(10) Clinical Result
1 ..	38	M	77	25	30	5	33	0	U
2 ..	50	M	58	25	25	4	40	0	I
3 ..	44	M	70	25	25	5	27	0	I
4 ..	40	M	73	20	20	6	3	2	I
5 ..	28	M	64	10	15	12	14	1	U
6 ..	60	F	54	20	25	11	8	0	I
7 ..	35	F	56	20	15	5	0	3	I
8 ..	37	M	80	20	—	—	—	—	—
9 ..	37	M	78	35	—	—	—	—	—
10 ..	43	M	64	35	35	6	2	2	I
11 ..	36	M	62	15	—	—	—	—	—
12 ..	56	F	62	15	—	—	—	—	—
13 ..	50	F	42	5	10	10	2	1	I
14 ..	55	M	68	25	—	—	—	—	—
15 ..	38	M	62	30	35	7	2	2	I
16 ..	43	M	97	30	—	—	—	—	—
17 ..	45	M	59	15	15	10	4	1	I
18 ..	47	M	82	35	30	6	9	0	I
19 ..	51	M	70	35	30	5	11	1	I
20 ..	51	M	73	30	25	3	5	1	I
21 ..	34	F	44	25	25	9	5	1	I
22 ..	35	M	70	25	—	—	—	—	—
23 ..	38	M	70	20	—	—	—	—	—
24 ..	59	M	53	20	15	6	4	0	I
25 ..	38	M	75	30	40	7	4	0	I
26 ..	45	M	66	20	—	—	—	—	—
27 ..	58	F	60	25	20	6	9	0	I

(one of more of the above changes). The interval between the last of the series of E.C.T. and the second determination of threshold was largely determined by events outside experimental control but in all cases it was as short as possible.

The E.C.T. procedure was identical in all cases. Atropine (1/100 gr.) was given subcutaneously 30 minutes beforehand, and thiopentone (200 mg.) and Scoline (30 mg.) were injected intravenously before the passage of current. This was delivered by a McPhail-Strauss Plexacon apparatus (30 joules, phase 2 for 30 seconds) and was followed by controlled breathing into a bag of pure oxygen, until spontaneous respiration was re-established. Most treatments were given twice a week, 7 being the average total (range 3–12). The patients were classified as "symptomatically improved or recovered" or as "failed to improve" at the time the post-E.C.T. EEG was recorded, 15 (11 men and 4 women) coming into the first category and 3 (2 men and 1 woman) into the second.

Eighteen patients had post-E.C.T. threshold determinations, the remaining 9 including 3 whose mental state was such that the psychiatrist in charge thought a repetition unwise and 6 who refused.

RESULTS

Column 5 (Table I) gives the threshold value before E.C.T., the mean for the whole group (27 patients) being 23 mg. hexazole. The mean threshold of the 6 females, 18 mg., is considerably lower than that of the 21 males, 25 mg.

The difference disappears if the threshold is expressed in terms of body weight (column 4), neither males, 0·36 mg./Kg., nor females, 0·34 mg./Kg., showing a significant difference from the group as a whole, 0·36 mg./Kg. The relationship between body weight and convulsive threshold suggested by this finding is shown in Figure 1, the correlation between them being positive and significant at the 1 per cent. level. The mean threshold for this group of depressive patients, 23 mg., is identical with that found (for the same end-point) by Ulett *et al.* (16) in a group of 27 subjects, 22 of whom were schizophrenic. A subsequent paper (14) from the same laboratory showed that the mean threshold for a group of 30 schizophrenic subjects was not significantly different from that of a mixed group of 20 non-schizophrenic and mental hospital patients. In this latter investigation the end-point taken was that of generalized myoclonus and the mean value (33 mg.) therefore appears higher than the figures found in the earlier paper and in the present study. However, if it is multiplied by the factor 23/31 suggested by Ulett's mean dose figures for various end-points the results are virtually identical. Comparison with the findings of other workers is difficult since leptazol (Cardiazol, Metrazol) has been used by most. Ulett's work suggests that for investigations of the present type hexazole is about 15 times as potent as leptazol weight for weight, and use of this factor gives a mean leptazol-equivalent threshold in the present series of 350 mg. or 5·5 mg./Kg., a figure which is comparable with that found in most published work, though low compared with Gastaut's original findings.

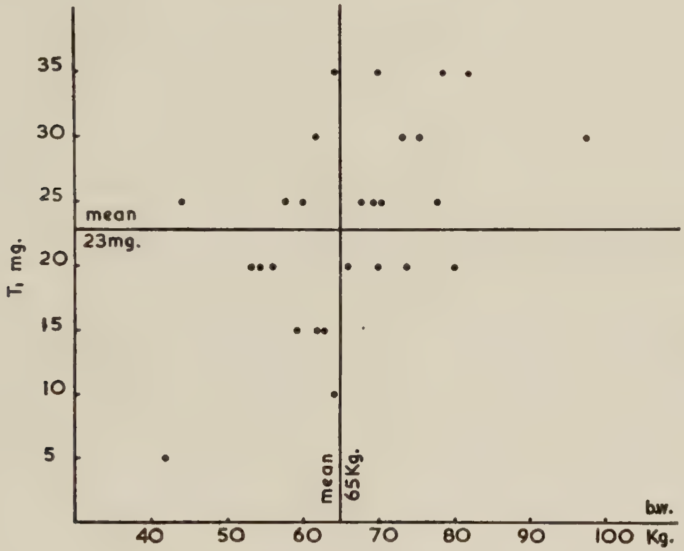

FIG. 1.—Crude threshold in mg. hexazole plotted against patient's body weight in Kg.

Column 6 (Table I) gives the threshold (T$_2$) values in those cases where satisfactory post-E.C.T. determination was possible. There is no significant difference between the T$_2$ means (13 males, T$_2$=26 mg.; 5 females, 19 mg.; total 18 patients, 24 mg.) and the T$_1$ means of the same 18 patients (26, 19, 24 mg. respectively) or that of the total 27 patients (given above). It appears probable that the difference found in any given patient between the T$_1$ and T$_2$

measures is within the limits of experimental error but as Figure 2 shows there is a tendency for those patients who had most therapeutic convulsions (column 7) to have a rise in threshold and for those with fewer E.C.T. to have a fall. On the other hand, there appears to be no relationship between the direction of change in threshold and the interval between the last induced convulsion and the second threshold measurement (column 8) even when the interval is small (Fig. 3).

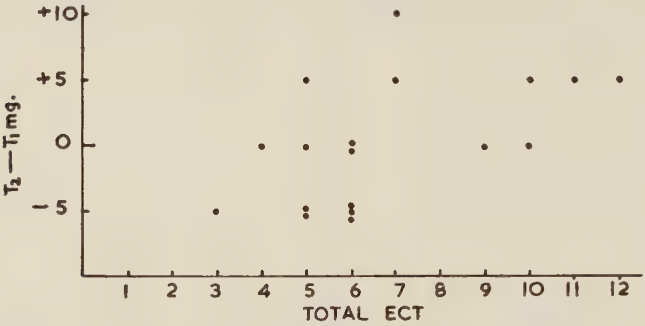

FIG. 2.—Difference between post-E.C.T. (T_2) and pre-E.C.T. (T_1) estimates of crude threshold plotted against total E.C.T. given.

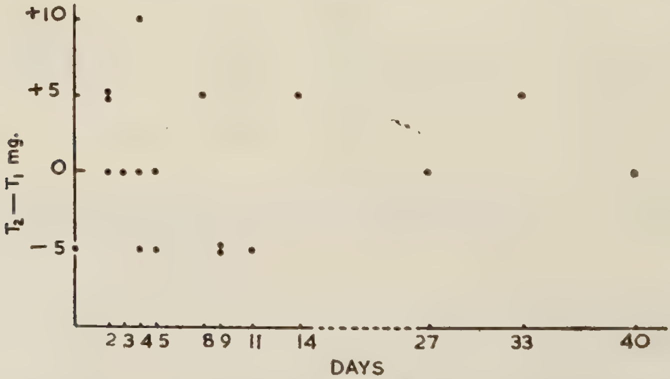

FIG. 3.—Difference between post-E.C.T. (T_2) and pre-E.C.T. (T_1) estimates of crude threshold plotted against the period in days between the last therapeutic convulsion and the post-E.C.T. determination of threshold.

The pre-E.C.T. EEG of each of the 19 patients having satisfactory T_2 determinations was normal and no abnormality arose following a 3-minute period of overbreathing or a series of rhythmic photic stimulations over a wide range of flash rates (1 to 30 f/sec.). The post-E.C.T. EEG in each case was placed in one of four categories according to the abnormalities found. These are given in column 9, Table I, the categories being: 0, no change, i.e. a normal record; 1, showing low voltage 6–8 c/s; 2, moderate voltage 4–6 c/s and 3, high voltage 3–6 c/s. ("Moderate" voltage representing roughly the amplitude of the alpha rhythm, "low" and "high" being about half and at least twice this.) As seen in Figure 4, there is a definite relationship between the "abnormality" of the post-E.C.T. record and the period since the previous convulsion, early post-E.C.T. records being the most abnormal. There is, however, no relationship between abnormality in the EEG and a change in convulsive threshold.

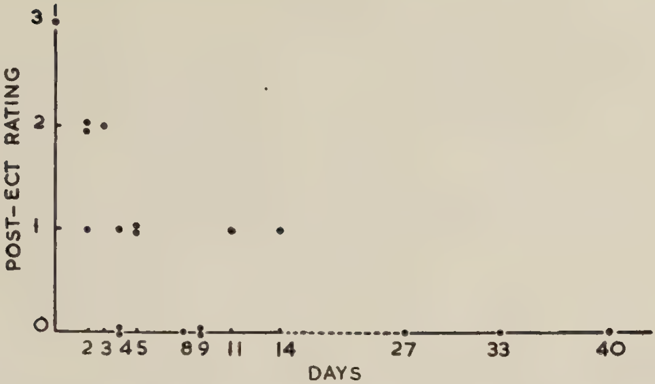

FIG. 4.—Post-E.C.T. rating (see text) plotted against the period in days between the last therapeutic convulsion and the post-E.C.T. determination of threshold.

Column 10, Table I, gives the short-term assessment of the patient's clinical state following E.C.T., the only 3 unimproved (U) cases showing no consistent difference in any variable from the remainder (improved, I).

DISCUSSION

The close similarity between the mean "threshold" in this group of 27 patients with depressive illness and that found by other workers in a wide variety of subjects—normal and abnormal—suggests that if psychiatric patients differ from each other and from the "normal" population neurophysiologically they do so in a way not susceptible to discovery by a single measurement of photoconvulsive threshold made under standardized laboratory conditions. It would appear, then, that the threshold has negligible clinical significance in its present form.

That there was no rise in threshold after a course of E.C.T. contrasts with the results of other workers. Leffman and Perlo (10) reported a rise in 4 schizophrenic patients, 2 of whom showed an initial elevation of threshold shortly after E.C.T., but a return to the original level a month later. Brockman *et al.* (3), in a larger series of chronic paranoid schizophrenic patients, found that a significant increase in threshold followed a course of 12 convulsions whether the latter were induced by "photo-shock" or conventional "electro-shock" methods. The greater change (increase from 31·2 to 75·6 mg. hexazole) was following "photo-shock" therapy, the lesser (increase from 30·5 to 49·7 mg. hexazole) following E.C.T. Several points deserve attention in comparing these findings with those reported in the present work. The increase in threshold found by both groups may be related to a failure in schizophrenia of a homeostatic mechanism which remains intact in depressive patients. However, as the larger series showed no difference between improved and unimproved patients with respect to threshold changes it is unlikely that this is an adequate reason.

A further point of importance is the possible influence of the number of convulsive seizures upon threshold change. Each of the Brockman *et al.* series had 13 seizures (one for threshold measurement and 12 therapeutic) before the final estimate of threshold, i.e. a much greater number than those of the present work (range 3 to 12, mean 7). It may be that the function measured is affected by convulsant therapy but only as a result of cerebral changes secondary to the convulsions. As seen in Figure 3 there is a tendency in the present work for those patients with the greatest number of E.C.T. to have higher second (T_2) than first (T_1) thresholds but the rise is very small compared with that found by Brockman *et al.*

Lastly in this connection is the difference in techniques used to measure "threshold" and the difficulty in strict comparison of results that arises. Brockman *et al.* estimated the amount of drug (hexazole) needed to produce an EEG or clinical end-point (myoclonus) in each case but the "convulsive threshold" as given in their results was determined by a different technique, a single large injected dose being followed by a continuously flashing stimulus until a generalized convulsive seizure occurred (additional injections being given if necessary). Although Ulett *et al.* showed that there was a high correlation between the amount of convulsant drug needed to lead to a valid "end-point" and the amount needed to produce a generalized epileptic seizure no evidence was presented that the latter arises simply by an increase in the intensity of the former. The fact that consciousness is lost in the major seizure suggests that a qualitative change in cerebral activity has taken place and it appears possible that the ease or otherwise of inducing this change may be affected by a number of shock therapies whereas the usual "end-point" phenomena are less affected.

That it is diencephalic function which is assessed quantitatively by the photoconvulsive technique was suggested by Gastaut following estimations of threshold in psychiatric patients (5) and experiments on laboratory animals (6). The work of Starzl *et al.* (15) and Hunter and Ingvar (8) indicated that in the cat under metrazol the visual cortex was responsible for the rapid spread of irradiated responses to the rest of the cortex. The diencephalon was involved only as part of a slower pathway. Similar experimental evidence is unlikely to be available in human subjects and the validity or otherwise of Gastaut's hypothesis can be determined only indirectly.

The neurophysiological effects of E.C.T. are not known with certainty, but subcortical rather than cortical structures are predominantly involved (1, 7). The effects of E.C.T. on the EEG—especially in relation to subsequent intravenous injection of thiopentone—suggest that the site of action of E.C.T. is the diencephalon (12, 13). If this is so the present finding, that no change in "threshold" follows E.C.T., offers some evidence that the pathway concerned in the measurement of threshold, though not necessarily that demonstrated in cats, is not affected by a change in diencephalic function.

SUMMARY

Estimation of photoconvulsive threshold was made in 27 patients with a severe depressive illness. The findings did not differ from those reported elsewhere in other psychiatric categories and normal subjects.

It was concluded that the threshold had no clinical differentiating value.

The estimation was repeated in 18 patients after a course of electroconvulsive therapy. No change in threshold was observed.

It was concluded that although no positive evidence of primary cortical involvement in the photoconvulsive mechanism was available it was unwise to assume that any aspect of diencephalic function was assessed by an estimate of the photoconvulsive threshold.

ACKNOWLEDGMENTS

The authors thank the consultant staff of the Maudsley Hospital for allowing access to their patients, the registrars for their co-operation, Dr. Denis Hill for advice in planning the work, Miss K. Spink for technical assistance and the Mental Health Research Fund for a financial grant.

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PERSONAL BACKGROUND, EMIGRATION AND MENTAL DISORDER IN HUNGARIAN REFUGEES

By

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Attention has been focused on the ecological aspects of mental illness since Faris and Dunham (1939) showed a higher incidence of schizophrenia in the centre of Chicago than in its peripheral parts. Earlier, Ødegaard (1932) had described a disproportionately high rate of psychotic breakdowns in Norwegian immigrants to Minnesota and in those who had returned to their homeland after a period of time in the U.S.A.

Malzberg (1940) found a steady progression in the relative incidence of mental diseases with increasing size of population; in particular, the standardized rate of first hospital admissions for schizophrenia was nearly twice as high in the largest cities as in rural districts. More recently, Ødegaard (1945) has analysed the distribution of mental diseases in Norway and has shown that migrants have considerably lower admission rates than those who have remained resident in their community of birth, with the exception however of migrants into Oslo, the capital and largest city, whose rate of hospital admissions was higher than for either of the other two groups. Malzberg and Lee (1956) found that the incidence of schizophrenia in New York State is very considerably higher in migrants, whether foreign or native-born, than in those born in the State.

This brief review of literature indicates that international migrations and, within the same country, centripetal migrations are associated with a higher rate of psychiatric illness, in particular schizophrenia. Concordant as these observations are, their interpretation—and relevance to the aetiological problem in schizophrenia—remains controversial. It has been argued (Faris and Dunham, 1939) that cultural isolation in the "socially disorganized" parts of the city plays a casual role (the "breeder" hypothesis), but others (Ødegaard, 1932) have expressed the view that the migratory process reflected the prepsychotic person's attempt to free himself from social ties and thus solve or evade existing conflicts (the "selection" or "segregation" hypothesis). It has been felt (Hare, 1956) that a study of the history and personalities of the patients might enable one to apportion the relative merits of these interpretations.

The literature hitherto quoted is either based on exclusively statistical data (e.g., Malzberg, 1940) or the retrospective study of an extensive case-note material (e.g., Ødegaard, 1932) where the length of time elapsed since the migration was not always explicit, and the patient's motive for it could not be examined. The recent arrival in England of several thousand Hungarian refugees (after the unsuccessful Hungarian uprising of November, 1956) offered an opportunity to study in detail the earlier life circumstances, and the events surrounding and following the emigration, in cases referred to a special psychiatric clinic for Hungarian refugees at the Maudsley Hospital. We hoped that an analysis of personality and environmental factors might permit of more definite conclusions than hitherto possible regarding the relationship of these to different forms of mental illness. It was postulated that, if the "selection" hypothesis accounts for the higher incidence of schizophrenia in immigrants, those who break down with this form of mental illness should be distinguishable in terms of their pre-emigration characteristics.

CASE MATERIAL

The data relative to 82 consecutive Hungarian refugees, referred for psychiatric disorders from 1 February, 1957, to 31 January, 1959, have been analysed. The large majority of these cases have been examined at the Maudsley Hospital, but a few were seen elsewhere at the request of other hospitals or Government agencies. The age and sex distribution, and the clinical features of these cases have been described elsewhere (Mezey, 1960). For the purposes of this investigation the case material has been divided into four groups according to diagnosis: (1) Schizophrenic disorders, including schizo-affective illness and paranoid states, 14 cases; (2) Affective disorders, including depressive states (Garmany, 1958) and a single case of hypomania, 23 cases; (3) Personality and neurotic disorders (Mayer-Gross, Slater and Roth, 1954), 41 cases; and (4) Organic disorders, including one case of mental deficiency, 4 cases.

The patients were referred by hospitals, general practitioners, Refugee Welfare organizations, official channels, and there were a few cases of self-referral. To exclude selection bias, the patients were compared in respect of their mode of referral (Table I).

The initial interview and examination took two hours on the average and it was endeavoured in every case to obtain independent information regarding history and symptomatology of the patient. Relatives and friends were interviewed and further information was sought from Hungary through correspondence with relatives and hospitals. The information obtained was graded satisfactory if independent account could be obtained about the most important points of history, and incomplete if the independent information available covered only a small period of the patient's life, or none was available. Satisfactory information was thus collected in 65 cases (79·2 per cent.) and the history remained essentially uncorroborated in 17 cases (20·8 per cent.) (Table I).

The age and sex distribution of the patients for the four diagnostic groups is given in Fig. 1.

RESULTS

Childhood and Marital Status

Disruption of family life before the end of adolescence, with its social and psychological consequences, is believed to be associated with a high incidence of abnormal personality development and delinquency. Its relationship to other forms of mental disorder is more controversial. Thus Lidz and Lidz (1949) found that 40 per cent. of a group of schizophrenics had been deprived of at least one parent before their 19th birthday, as opposed to only 17 per cent. of their normal control group. Oltman, McGarry and Friedman (1952) have examined their problem on a much larger case material and found that about one-third of schizophrenics, manic-depressives and normal controls have all had a history of "broken home", while the proportion rose to nearly one-half of cases among psychopathic personalities and psychoneurotics.

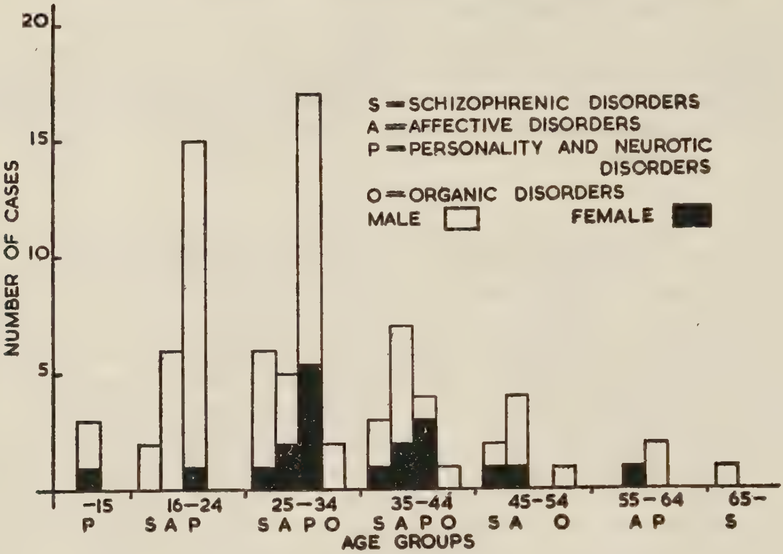

FIG. 1
Age and sex distribution of the patients for the four diagnostic groups.

On account of the difference in the cultural background, the age of 16 was taken as the end of adolescence for our Hungarian patients, and broken home defined as withdrawal of one or both parents before attaining this age, owing to the death of one (19 cases) or both parents (3 cases), divorce or separation of parents (5 cases) and illegitimacy and/or institutional upbringing (6 cases) (Table I).

Ødegaard (1946 and 1953) has conclusively shown that the much higher incidence of mental diseases in the single than in the married is due primarily to "selection by marriage", certain personality traits reducing the chances of getting married. The death of the spouse does not lead to any considerable change in this positive selection, while in the divorced the incidence of psychosis is nearly as high as in the single. The marital status of our patients was: 42 single, 18 married, 4 widowed and 18 divorced or separated (Table I).

Previous Migratory Record

Studies of internal and international migrations have been pursued independently and we wished to investigate on this case material the relationship between the previous migratory record in Hungary of our patients, and their subsequent migration abroad.

Residence at birth of our patients was Budapest, the capital, in 42·7 per cent. of cases, and elsewhere in Hungary in the remainder. The majority of patients (66·9 per cent.) resided in Budapest at the time of their leaving Hungary and only 33·1 per cent. were living in other parts of the country (Table I).

Slightly more than half (52·1 per cent.) of our cases had migrated from one part of Hungary to another, the rest having stayed until the time of emigration at the place of their birth. Among those who had migrated, 23 patients went to live in Budapest, and 14 migrated from one country area to another, or from Budapest to the country. In view of the differential psychiatric morbidity depending on the direction of migration found by Ødegaard (1945)

TABLE I

		Schizo-phrenic Disorders	Affective Disorders	Personality and Neurotic Disorders	Organic Disorders	χ^2 (d.f. = 3)	p<
Mode of referral	Medical (or self)	8	16	16	2	5·73	N.S.
	Welfare (or official)	6	7	25	2		
Satisfactory independent information	Yes	12	14	35	4	3·85	N.S.
	No	2	9	6	–		
"Broken home"	Yes	4	8	19	2	1·87	N.S.
	No	10	15	22	2		
Marital status	Single, divorced or separated	11	13	33	3	1·18	N.S.
	Married or widowed	3	10	8	1		
Residence at birth	Budapest	2	11	21	1	6·47	N.S.
	Provincial	12	12	20	3		
Residence on emigration	Budapest	9	18	24	2	1·54	N.S.
	Provincial	5	5	17	2		
Direction of previous migration	To Budapest	9	7	6	1	11·6	0·01
	Other (or none)	5	16	35	3		
Emigration previously considered	Yes	—	8	9	1	5·49	N.S.
	No	14	15	32	3		
Motive for emigration	Political (or partly political)	2	10	28	3	17·81	0·001
	Non-political	12	13	13	1		
Companion in emigration	Relative or friend	3	9	13	1	1·12	N.S.
	None	11	14	28	3		
Fall in social class	0	11	17	29	3	·23	N.S.
	1	3	6	12	1		

in Norway, we divided our patients into those who had migrated from the country into Budapest, and those whose previous internal migration was in another direction, or who had no previous record of migration. The differences between the groups are highly significant and showed a high number of schizophrenics who migrated to Budapest (Table I).

Motivation for leaving Hungary

All these patients had left Hungary during, or immediately following, the uprising of November, 1956. It could not be assumed, however, that they had all left their country for political reasons. Since the beginning of this century, at least, a steady stream of emigrants have left Hungary for the countries of the West, particularly the United States. In 1913 this emigration reached its peak with 117,580 voluntary migrants to the U.S.A. alone within a calendar year, from the then territorially much larger Hungary (Epstein, 1914). Between the two world wars this emigration was artificially kept in check by limitation of intake in the countries of destination (in particular, the quota laws of the U.S.A.), and after the second world war through the great difficulties of leaving the country of origin by legal means. However, the process of westward migration was never entirely halted. The revolutionary period, which swept away the local hindrances to emigration and, at the same time, created greater willingness in the countries of destination to admit Hungarians, offered a favourable opportunity to leave for all those who might have emigrated in any case, circumstances permitting. Hoff and Strotzka (1958) distinguished four different groups of Hungarian refugees according to their reasons for emigration, only one of them being political; they did not give, however, quantitative data regarding the relative size of these groups. It has been estimated (Hinkle, 1958) that before the start of the uprising more than 50 per cent. of refugees had considered leaving Hungary at the first opportunity. We have systematically inquired in every case about the circumstances leading to emigration and, in particular, we have tried to establish whether it was planned or considered before the uprising, or whether it was born of the situation reigning at the time of the internal upheaval. Although none of our schizophrenic patients contemplated emigration prior to the uprising, the differences between the groups remain just short of statistical significance (Table I).

We have further tried to elicit in every case the reasons that prompted the decision to leave Hungary. The answers given were divided into Political, Partly-Political and Non-Political Motivation. The Political motivation (28 per cent. of cases) included cases where the patient had taken no part whatsoever in the uprising, and sometimes even lived in a part of the country not touched by it, but who had political objections to the régime or had to suffer from its economical or other consequences; in the same category belong certain Jewish patients alarmed by the renewal of anti-Semitism in the revolutionary period. Non-Political Motivation (55 per cent. of cases) included Economic reasons (unconnected with political opposition to the régime),) e.g. to work in the West traditionally regarded as offering a higher standard of living, Domestic reasons, e.g., to escape from a father regarded as a bully, to avoid paying maintenance to an estranged wife, to put an end to an intolerable marital situation, etc., and Personal, which included a large variety of reasons from seeking adventure and seeing the world to looking for more efficient medical treatment (a case of Myasthenia gravis), and purely chance decisions without forethought or apparent reason. The frequency of these different motivations between the diagnostic categories is very significantly different (Table I). Elimination of the schizophrenic group from the statistical comparison reduces the probability below significance ($\chi^2 = 4 \cdot 14$; d.f.$=2$; $p < 0 \cdot 2$), thus proving that the significance is due to the discrepancy between observed and expected scores in schizophrenics.

The patients were divided into those who had left Hungary in the company of a relative or very close friend, and those who undertook emigration alone, or accompanied only by chance acquaintances. The diagnostic groups do not differ significantly in this respect (Table I).

Social Mobility

The relationship beween social structure and mental illness has been the subject of several recent investigations (Hollingshead and Redlich, 1954 and 1955; Hare, 1955; Ødegaard, 1956; Stein, 1957). In a considerable proportion of cases the situation of a recent immigrant is that of a *déclassé*, and we wished to investigate the bearing of this downward social mobility on the different diagnostic groups of our case material.

Because of the differences in the socio-economic and political structure of the two countries, certain occupations do not carry corresponding prestige or financial rewards. In order to avoid gross errors of classification we have therefore grouped our patients in three large social classes; these were Class A, analogous to Class I, Class B, corresponding to Classes II and III, and Class C, corresponding to Classes IV and V of the Registrar-General's Classification. The social class distribution of our patients in the two countries was as follows:

TABLE II

Social Class	Schizophrenic disorders		Affective disorders		Personality and neurotic disorders		Organic disorders	
	Hung.	Eng.	Hung.	Eng.	Hung.	Eng.	Hung.	Eng.
Class A ..	1	–	3	1	–	–	–	–
Class B ..	6	4	16	12	22	12	2	1
Class C ..	7	10	4	10	19	29	2	3

The four diagnostic categories did not differ significantly in the frequency of their respective social mobility (Table I).

Social Adaptation

Adaptation or adjustment is a term of many meanings (Kahn, 1938; Lewis, 1953) and is sometimes used indiscriminately in psychiatric literature. For the purposes of this paper we have adopted the operational definition of Barrabee, Barrabee and Finesinger (1955), according to which, an individual is adjusted if he is satisfactorily fulfilling the normative social expectations of his role as husband, father, worker, etc., and independently of whether he regards them as entirely satisfactory. Social adaptation was rated in seven areas (Family, School, Sexual, Marital, Work, Social and Recreational, and Community) following the criteria of Brill and Beebe (1955). We have assessed the relative degree of maladaptation of every patient, both in Hungary and in England, in order to compare the change subsequent to migration abroad and its possible relevance to the causation of the particular form of mental illness here investigated.

TABLE III

Areas of Maladaptation	Schizophrenic disorders		Affective disorders		Personality and neurotic disorders		Organic disorders	
	Hung.	Eng.	Hung.	Eng.	Hung.	Eng.	Hung.	Eng.
Family ..	3	1	3	2	19	8	–	–
School ..	5	–	2	–	18	1	1	–
Sexual ..	5	5	7	12	13	16	–	–
Marital ..	3	3	7	2	12	7	1	–
Work ..	4	2	1	4	21	26	2	–
Social and Recreational	5	8	1	11	24	29	–	1
Community ..	1	2	1	1	9	11	1	1
Totals ..	26	21	22	32	116	98	5	3

It is only the patients suffering from affective disorders whose apparent social adaptation deteriorates and might be presumed to play a part in the aetiology of their illness. The increase in maladaptation of these patients is due to difficulties in social and recreational activities and, to a lesser extent, in work and sexuality.

The assessment of social adaptation by counting the areas in which it is defective might prove misleading; if a patient has reduced the number of maladapted areas by the very fact of emigration (e.g., separation from family) or by the ordinary process of growth (e.g., after leaving school) the improvement registered in social adjustment is spurious. Thus the diminished total figure for maladaptation in England, as compared with Hungary, in schizophrenics and personality disorders can be accounted for by the difference in the respective scores for adaptation to school. To avoid this source of error we have devised an Index of Social Adaptation (I.S.A.).

Method

The patient's adaptation is rated either "good" (or "adequate"), or "poor" for all areas where rating is appropriate, and the Index is calculated from the ratio of the number of maladapted areas to the number of areas where adaptation was rated. Examples:

Mr. L.V., aet 34. *Diagnosis*: Depressive Illness. *Social adaptation in Hungary*: *Family*: good. *School*: good. *Sexual*: good. *Marital*: good. *Work*: good. *Social and Recreational*: good. *Community*: good. *I.S.A.*: Number of maladapted areas/Number of areas rated=0/7=0. *Social adaptation in England*: *Family*: (left in Hungary). *School*: —. *Sexual*: poor (constant preoccupation). *Marital*: (wife left in Hungary). *Work*: good. *Social and Recreational*: poor (avoids social contacts). *Community*: good. *I.S.A.*: Number of maladapted areas/Number of areas rated=2/4=0·5.

Mr. H.S., aet 42. *Diagnosis*: Chronic mixed neurosis. *Social adaptation in Hungary*: *Family*: poor (conflict)). *School*: good. *Sexual*: poor (frigidity). *Marital*: poor (divorce). *Work*: adequate. *Community*: good. *I.S.A.*: Number of maladapted areas/Number of areas rated=3/7=0·42. *Social adaptation in England*: *Family*: poor (insulting behaviour). *School*: —. *Sexual*: poor (frigidity). *Marital*: —. *Work*: adequate. *Social*: adequate. *Community*: good. *I.S.A.*: Number of maladapted areas/Number of areas rated=2/5=0·40.

The difference in mean I.S.A. in Hungary distinguishes significantly Affective from Schizophrenic disorders (S.E.$=0{\cdot}072$; $t=4{\cdot}58$; $p<0{\cdot}001$), Affective from Personality (and neurotic) disorders (S.E.$=0{\cdot}068$; $t=3{\cdot}48$; $p<0{\cdot}001$), as well as Schizophrenic from Personality (and neurotic) disorders (S.E.$=0{\cdot}091$; $t=2{\cdot}54$; $p<0{\cdot}02$).

The change in the means of I.S.A. subsequent to emigration for the different groups is given in the following table:

TABLE IV

Diagnostic Category	Hungary	England	Difference	S.E.	t	p<
Schizophrenic disorders ..	0·271	0·39	0·119	0·08	1·49	0·2
Affective disorders ..	0·171	0·311	0·14	0·053	2·64	0·02
Personality & neurotic disorders ..	0·501	0·569	0·068	0·025	2·72	0·02

By this method the deterioration of social adaptation in affective disorders is confirmed: the ratio of maladapted areas to total number of areas rated increasing from about 1/16 to nearly 1/3, a statistically significant difference. The difference in the means of the Indices for the two countries is more discrete in the schizophrenic group, the respective ratios being approximately 1/4 and 2/5, and not significant. The deterioration in adaptation subsequent to emigration, as measured by the rise of the Index of Social Adaptation is actually very small for personality and neurotic disorders—from 1/2 to 10/18 approximately—but nevertheless statistically significant.

DISCUSSION

There was a history of early disruption of the home in 40 per cent. of Hungarian refugees referred for psychiatric disorders. In the absence of comparable data, it is not possible to evaluate the significance of this figure. The only reference we were able to find was one reporting a history of broken home in 54 per cent. of cases of accident-prone patients in Budapest (Csillag and Hedri, 1949). Whether the percentage of this family constellation is characteristic of Hungarian refugees with psychiatric disorders, or for the parent population as a whole, it remains that within our case material the differences between the diagnostic groups were not significant.

Our case material also appeared fairly homogeneous in respect of marital status. This statement has to be qualified, however, as available numbers did not allow detailed statistical analysis, and marital status had to be examined in two large categories of (a) single, divorced or separated, and (b) married or widowed. Furthermore, the figures were not standardized for age.

A comparison of the previous migratory record of these patients revealed a relationship between the direction of their earlier migration in Hungary and the type of psychiatric disorder they were suffering from when seen in England. While there was no significant difference between the groups regarding their Hungarian residence at birth, or immediately prior to emigration, schizophrenic patients had emigrated from the country to Budapest in a significantly higher proportion of cases than those belonging to other diagnostic categories.

The study of our patients' motivation for leaving Hungary shows interesting features. Only 22 per cent. had previously planned, even vaguely, to emigrate, and in the remainder this important decision was born in the chaotic circumstances of the uprising. In particular, none of the schizophrenic patients had earlier contemplated going abroad. However, the difference between the groups remains short of the usual criterion of statistical significance. The immediate motive for leaving Hungary was political, or partly political, in about 45 per cent. of cases. When the figures were statistically analysed, the frequency of non-political motives was significantly higher in those having a schizophrenic illness than for other diagnoses.

A fall in social class subsequent to emigration was observed in more than a quarter of our cases, but its frequency was not significantly different between the groups. It will be appreciated, however, that the method of social classification adopted, while necessary in the interests of accuracy, was of a type likely to mask finer differences in social mobility.

The comparative analysis of the social adaptation of our patients, before and after emigration, showed that those with affective disorders had suffered a considerable, and statistically significant, deterioration, while the Index of Social Adaptation of schizophrenics in England did not significantly differ from their earlier Hungarian Index. Except in affective disorders, it is difficult therefore to ascribe aetiological importance to the stresses of emigration in the causation of the psychiatric disorders of our patients. Sociologists have used the evocative terms of "marginal men" (Park, 1928) and "stranger" (Schuetz, 1944) to describe the predicament of the migrant, faced with a dislocation of his habitual system of reference. Our data do not lend support to the thesis (Faris, 1934) that cultural isolation subsequent to migration plays a decisive part in shaping the schizophrenic personality; the assessment of the pre-migratory social adaptation in these cases showed that they tended to be "marginal" people already in Hungary. The frequent history of earlier migration to Budapest, the predominantly non-political motives for emigration undertaken without any previous planning, indicated in fact that their maladaptation had been the major reason for leaving Hungary. In these respects they were clearly distinguishable from other diagnostic groups, confirming therefore the initial deduction from the "selection" hypothesis.

Summary

The family circumstances, previous migratory record, motives for emigration, social mobility and social adaptation of 82 consecutive cases of Hungarian refugees with psychiatric disorders, divided into four diagnostic categories, have been investigated.

The groups did not differ in respect of the frequency of a "broken home" background, marital status and the downward social mobility subsequent to emigration.

Schizophrenics differed significantly from other diagnostic groups in their higher previous record of migration from rural and provincial areas to Budapest, and the higher frequency of non-political motives for leaving Hungary. The mean Index of Social Adaptation deteriorated significantly in England for those suffering from affective disorders, but not for schizophrenics, and it is concluded that, in the two year period covered by the investigation, the stresses of emigration did not play an important causal role in schizophrenic illnesses.

These findings support the "selection" (or "segregation") hypothesis" in the interpretation of the differential incidence of schizophrenia in migrants.

ACKNOWLEDGMENTS

I wish to thank Dr. D. L. Davies, Dean of the Institute of Psychiatry, who made this study possible by offering facilities for a Hungarian Clinic. My thanks are also due to Dr. G. M. Carstairs and to Dr. E. H. Hare for criticism and advice; to Dr. A. E. Maxwell for help with the statistical treatment of the data, and Mrs. T. A. Maxwell for secretarial assistance.

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PSYCHIATRIC ILLNESS IN HUNGARIAN REFUGEES

By

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At the beginning of this century the high rate of "insanity" among immigrants was a matter of considerable concern in the U.S.A. and it has been used as one of the main arguments for curtailing immigration. The problem has been reviewed, and examined with modern statistical methods, by Ødegaard (1932) and Malzberg (1940).

It has been estimated that forty million people have become refugees since 1945 (E. Rees, 1957), and this has generated a renewed interest in this tragically topical problem. Considerable attention has been focused on the plight of Hungarian refugees (Hoff and Strotzka, 1958; Koranyi, Kerenyi and Sarwer-Foner, 1958; *The Hungarian Revolution of October 1956*, 1958), who have recently joined the millions of international migrants.

Between November 1956 and April 1957 about twenty thousand Hungarians were admitted into the United Kingdom (*Refugees in England*, 1958), and the medical problems arising from such massive arrival of refugees have been described by Dormandy, Eldon and Milner (1957). Previous papers (Frost, 1938; Kino, 1951; Murphy, 1955) have examined certain clinical and statistical aspects of psychiatric illness among immigrants admitted to mental hospitals in England, but Murphy (1952) has regretted the total absence of studies of neurosis in any refugee group in Britain. In addition, the refugees and displaced persons who have been the subjects of these studies came from diverse cultural backgrounds, have often lived for years in concentration camps with their attendant physical and psychological traumata, and have spent widely differing periods of time in this country before illness led to hospital admission. The Hungarian patients, on the other hand, were rather suddenly immersed from one cultural environment into another and it was possible to examine a relatively large number of cases of all forms and degrees of severity, breaking down in the first two years following their emigration. We propose to describe the clinical findings in this group of patients; the relationship of the personal background to the form of their subsequent illness will be discussed elsewhere (Mezey, 1960).

Case Material

It became obvious soon after the arrival of Hungarian refugees in the United Kingdom that the psychiatric care of those needing it was made particularly difficult by the language barrier. To deal with these cases, at the request of the Hungarian section of the British Council for Aid to Refugees, (B.C.A.R.), a temporary clinic conducted by an Hungarian-speaking psychiatrist was established at the Maudsley Hospital.

The data regarding the composition of the group of Hungarian patients here reviewed are summarized in Table I.

In a proportion of cases, the patient was initially seen by a psychiatric social worker employed by the B.C.A.R., and then by the writer at the

TABLE I

Distribution of patients with regard to mode of arrival to the U.K., referral for psychiatric care, residence on referral, source of information, religion, marital status and social class.

Mode of arrival to the U.K.	Bulk schemes for refugees	65
	Mining recruits	12
	Individual visas	5
Referred by	Voluntary and Governmental agencies	31
	General Practitioners	23
	Hospitals	21
	Patient (or his family)	7
Residence on Referral	London	62
	Elsewhere in England	20
Independent Information	Satisfactory	21
	Adequate	44
	Poor (or none)	17
Religion	Roman Catholic	52
	Protestant	14
	Jewish	13
	Other	3
Marital Status	Single	42
	Married	18
	Widowed	4
	Divorced or separated	18
Education	None	1
	Elementary	50
	Secondary	17
	Academic	14
Social Class (in Hungary)	Professional	4
	Intermediate and artisanal	46
	Labouring	32
Social Class (In England)	Professional	1
	Intermediate and artisanal	29
	Labouring	52

Maudsley Hospital. During the initial period, when the B.C.A.R. was in charge of the resettlement of Hungarian refugees, practically every case came through their intermediary, but later an increasing number were referred by other agencies, voluntary (e.g. denominational) or official (National Assistance Board, Prison Commission, etc.). As the refugees were leaving the hostels to settle in the community, they started to come mainly through medical channels. There were also a few instances of self-referral.

During the two-year period from 1 February, 1957, to 31 January, 1959, altogether 90 cases have been seen at this special clinic at the Maudsley Hospital. Of these, eight cases were excluded for the following reasons: in four the information obtained was insufficient (emergency cases or lack of co-operation), two were immigrants of a previous period and did not qualify for inclusion, and in two no psychiatric abnormality was found.

The present report is therefore based on observations in 82 consecutive cases of recently arrived Hungarian refugees with psychiatric disorders. These patients all arrived in England between November 1956 and April 1957. Nearly eighty per cent of them came under bulk schemes organized by the B.C.A.R., and the rest as mining recruits engaged by the National Coal Board or with individual visas.

This was the only clinic dealing specifically with this population and therefore the majority, if not the totality, of psychiatric problems among Hungarian refugees in the metropolitan area were referred to it. Nearly a quarter of cases, however, were referred from areas as far distant as Bristol and Fleetwood.

The age and sex distribution of patients is given in a histogram (Fig. 1). An age check of a random sample of Hungarian refugees taken from the Home Office Register (*Refugees in Britain*, 1958) showed that 84 per cent. of Hungarian refugees were between the ages of 18 and 40, as compared to only 65 per cent. in our sample. One-quarter of our group were females, males heavily outnumbering females in the 16-24 age group. The proportion of women in the Hungarian refugee population admitted to Britain is not known.

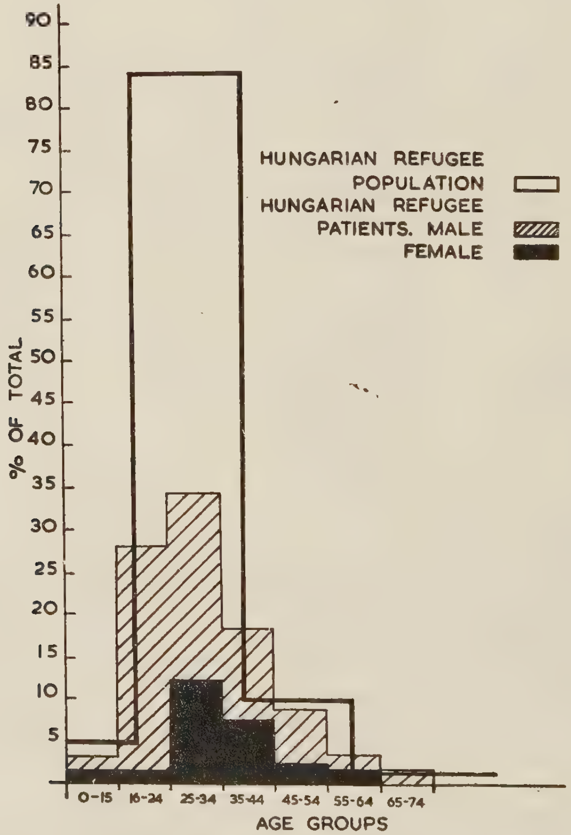

FIG. 1.—Age and sex distribution of Hungarian psychiatric patients, compared with the age distribution of a random sample of Hungarian refugees (*Refugees in Britain*, 1958).

For the proper evaluation of the history, it seemed important to supplement the information received from the patient by contacting his relatives, acquaintances and (in the case of previous psychiatric illness) hospitals, whether in England or in Hungary. Only in a quarter of the cases was it possible to have a complete history from independent sources; in more than half the information obtained from sources other than the patient himself covered the most important areas (personal relationships, previous illnesses and present symptoms) and only in about 20 per cent was outside information absent or very inadequate.

The majority of patients seen (60·3 per cent.) were, as expected, of the Roman Catholic faith and the remainder distributed among other denominations. Men greatly outnumbered women in all but the Jewish group (six men to seven women).

This was a predominantly young population and just over half of the patients were single. It is striking, however, that the number of divorced or separated patients equalled that of married people. Relevant data for Hungary, or for the total Hungarian refugee population in Britain are not available.

One patient of gipsy extraction (struck by severe paralytic poliomyelitis in early childhood) never had any sort of schooling; the majority partook of the compulsory elementary education until the age of 13.

About 30 per cent. of patients went to secondary school, and 17 per cent. had some form of superior education, not always completed. More than half of the patients were merchants, white collar or skilled workers in Hungary; a considerable proportion were labourers and less than 5 per cent. belonged to the professions. A frequent downgrading in social class was observed as characteristic of their occupational status in Britain.

HISTORY

The circumstances of the investigation were such that reliable information on the incidence (and nature) of *psychiatric illness in parents* and collaterals could not be expected, but the impression was that this was not unduly high.

There was a history of *previous mental illness* in half of our patients (Certain in 30, Probable or Possible in 11). To be classed in the Certain category, a patient had to have a history of admission to a mental hospital in Hungary, or of being treated as an outpatient for a disorder diagnosed as psychiatric. Previous psychiatric illness was considered Probable if the patient had a history of temporarily incapacitating disorder and either this was regarded by his medical attendants as possibly psychiatric or "nervous", or the mental and somatic symptoms of the previous illness were practically identical, in the view of the patient or other informants, to those for which he was referred in England. The criteria for Possible psychiatric illness were similar, but in these cases the information at disposal was usually less complete or reliable.

Mrs. I.S., *aet.* 43. Referred from another hospital, where after pulmonary resection for tuberculosis, she developed florid ideas of significance and of reference, irritability and violent fluctuations of mood. Since the age of 12 she had been subject to periods of incapacitating mental illness, each of a few months' duration; in the earlier attacks mostly anxiety and its somatic concomitants, later fatigue, depression, paranoid delusions and marked agitation. Since the age of 30 admitted on at least three occasions to mental hospitals, for periods up to ten months. Treated with deep insulin, repeated courses of electro-shock and drugs. Considered unfit for work during last three years. Previous psychiatric illness Certain.

Mr. J.M., *aet.* 32, hairdresser. Complains of severe headaches, pressure in throat, palpitations, pain behind the eyes. Extensively investigated in two London teaching hospitals, along somatic lines. N.A.D. and referred for psychiatric opinion.

First similar illness in 1954. Investigated in Budapest where all findings, including B.M.R., were within normal limits. In view of the subjective respiratory difficulties, the diagnosis of retro-sternal goitre was made and thyroidectomy performed. Subsequent periodic recurrence of same symptoms. Previous psychiatric illness Probable.

Mr. G.F., *aet.* 30, civil engineer. Referred by his employer for abnormal behaviour at work. Believes he is suspected of being a Communist spy, he is followed in the streets, his room is searched in his absence, his colleagues are jealous because of his promotion and make subtly disparaging remarks, etc.

Two previous illnesses, in 1952 and 1954, of indefinite character. Morose, uncommunicative, irritable and unable to work for several weeks. Refused to see a psychiatrist, or indeed any doctor, although advised to do so. Previous psychiatric illness Possible.

The *onset* of the present illness was acute (duration less than three months) in 38 cases, subacute (duration on referral between four and twelve months) in 25 cases, and chronic (duration over one year) in 19 cases.

Clinical Findings

The *leading symptom* (Table II) was most often physical, either in the sense of the somatic manifestations of anxiety and depression or a hysterical disorder of function. Tyhurst (1951) has made similar observations in displaced persons settling in Canada. In view of the difficulty in communicating with these patients, it is not surprising that they were often subjected to manifold clinical, laboratory and radiological investigations before the psychiatric nature of the illness was suspected.

Table II

Distribution of the leading symptoms in Hungarian psychiatric patients

Somatic complaints	23
Abnormal behaviour	22
Delusion	12
Suicidal attempt	9
Disorder of function	5
Fear and/or depression	3
Antisocial act	3
Social incompetence	3
Disorder of consciousness	2

Abnormal behaviour was the next most common presenting symptom; this took a variety of forms, from aggressive outbursts to wandering, and from suicidal threats to smearing of faeces on lavatory seats. In the majority of schizophrenics the presenting symptom was delusional, sometimes inseparable from hallucinatory experiences. A suicidal attempt of variable severity, and sometimes repeated, was the leading symptom in nine cases.

Rarely, and only in patients who have previously been under psychiatric treatment, was the initial symptom expressed in psychological terms such as anxiety or depression. A small number of cases were referred for antisocial acts (one after homicide, two for stealing). In three cases the immediate reason for referral was the inability to obtain or hold employment. Finally, two patients came for intermittent disorder of consciousness (a dissociative state and a case of traumatic epilepsy).

The distribution of patients according to *diagnosis* is given in Table III. We have used four main diagnostic categories; the subdivisions within these were inevitably arbitrary and the designations meant to indicate the clinical form of the illness when observed, rather than to describe an independent entity.

The most frequent form of schizophrenia was the paranoid. In many cases the delusional ideas were bearing the mark of recent experiences and of the present life situation of the patient: feeling accused of being a Communist spy, or being persecuted by ubiquitous Communist agents. Hallucinated voices, when reported, were often said to speak in English and in these cases the patient had no doubt about their derogatory meaning, although they were

TABLE III

Distribution of Hungarian psychiatric patients according to diagnosis

Schizophrenic Disorders: 14	*(17·07%)*
Paranoid schizophrenia	9
Hebephrenic schizophrenia	1
Schizoaffective illness	1
Paranoid state	2
Paraphrenia	1
Affective Disorders: 23	*(28·04%)*
Depressive illness	13
Anxiety state (with depression)	9
Hypomania	1
Personality and Neurotic Disorders: 41	*(50%)*
Abnormal Personality	15
Hysteria (sensory or motor)	13
Mixed neurosis	6
Behaviour disorders of childhood or adolescence	4
Obsessional illness	1
Psychasthenia	1
Homosexuality	1
Organic Disorders: 4	*(4·87%)*
General paralysis	1
Alcoholic hallucinosis	1
Traumatic epilepsy (with personality change)	1
Mental defect (low grade)	1

clearly incapable of understanding conversational English. Certain patients sought to escape from these hostile influences by further emigration and two wanted to return to Hungary. The majority of cases were indistinguishable in form or content from schizophrenic illnesses observed in Western countries. There was one case of schizoaffective illness who presented a particularly interesting clinical picture of paranoid illness superimposed on marked mood swings. One of the two cases described as paranoid state was suffering from delusions and a profusion of ideas of significance in a setting of severe anxiety, followed by an apparently complete recovery. The other was the passive member of a "folie a deux" partnership, the active partner suffering from paraphrenia.

An agricultural labourer, *aet.* 66, and his wife, *aet.* 51, had left their hostel after multiple scenes in which they accused the other refugees accommodated there of insulting behaviour. For several days they were roaming the streets, without adequate nourishment and sleeping in parks, until picked up by the police and admitted to an observation ward. The wife was agitated, shouting at the top of her voice; she had firmly fixed delusions about the execution of her son (he stayed in Hungary) which she believed she had witnessed in England, and her own impending execution: auditory hallucinations and ideas of reference were present. The husband appeared quiet, rather depressed, sharing the wife's delusions about the period preceding admission to hospital, but denying similar experiences since then. Neither spoke any English. They had been married for 27 years and the wife had always been known for her domineering personality.

Affective disorder was diagnosed in 23 patients. In all but one, the mood was of unpleasant quality, both anxiety and depression being present in a proportion varying from case to case. The majority of these patients described their illness in somatic terms. The climate in Britain, so different from the central European, was often blamed for these symptoms. Anxiety state was diagnosed when these complaints were mobile and of a type regarded as a physical accompaniment of anxiety. Depression was diagnosed when the patient reported characteristic disturbances of sleep, appetite, weight or libido, or when his somatic complaints reflected his preoccupation with catastrophic illness. Separation of depressions into exogenous and endogenous seemed neither possible nor justified (Lewis, 1934; Garmany, 1958). Guilt, unworthiness or hopelessness were only rarely referred to in these terms, but the patients frequently regarded themselves as in some way responsible for their present predicament and sometimes sought a way out through self-destruction. As a whole this group showed a marked tendency to idealize the past, and this was associated with a mistrustful or resentful attitude toward the present environment. Several patients expressed regret for having left their country, a decision which they now regarded as hasty and inspired by general panic; with few exceptions, however, emigration was accepted as an irrevocable fact.

Mr. Z.H., *aet.* 24, a teacher of Russian in Hungary. Referred by B.C.A.R. Was not opposed to the régime, but let himself be persuaded into emigration by a friend. Difficulties in getting any but labouring jobs. Feels tired, tensed up. Ruminations about the future ("What will happen to me this year, next year", etc.). Blames the damp weather ("I cannot live in this country, it is affecting my soul"). Feels inadequate ("I am no good, I am very stupid and won't get anywhere"). Preoccupied with death and very apprehensive ("Everything fills me with forebodings"). He does not think that returning to Hungary or emigrating would solve his difficulties: he believes in fact that there is no remedy for them. Disturbed sleep with early waking. Loss of libido. Often weeps spontaneously.

Exactly half of our patients were diagnosed Personality and Neurotic disorders (Mayer-Gross, Slater and Roth, 1954). In this group the most frequently observed form was behavioural abnormality, often in the antisocial sense. Sensory and motor hysteria were seen in classical form—functional blindness, aphonia, paralysis, fits—much more commonly than in the local population. These "conversion" symptoms were particularly frequent in patients with low intelligence.

M.F., *aet.* 23, hotel porter. Admitted to a general hospital after being found in a dazed condition in his lodgings. On admission he was conscious, with rolling eyes and hyperventilation. He complained of unbearably severe pain around the scar (an old meniscectomy) on his left knee. Two nights after admission he became uncontrollable and very noisy. He was groaning, rolling about the bed and over-breathing so much that he produced tetany. On medical and orthopaedic examination no abnormality was found to account for his symptoms, except for some tender nodules under the operation scar. Referred for psychiatric opinion.

Always a solitary boy, very attached to his mother. Poor scholar. At the time of the uprising he was serving in the Hungarian Air Force, away from home. He came abroad following the example of other soldiers, without an opportunity to consult his parents or any definite idea of what he wanted to do. Since his arrival in England as a mining recruit he felt unhappy and wanted to return home. Left miners' hostel and came to London, but received a letter from his mother strongly advising him against returning to Hungary. Three days later, onset of symptoms described. On examination he appeared to be of very low intelligence, and this was confirmed by testing (below the 25 percentile rank on the Progressive Matrices Test). No delusions or hallucinations. Poor general information. Hyperventilation during psychiatric examination, readily stopped. Two days later he declared that the pain had gone and he left the hospital against advice.

The majority of hysterical patients exhibited marked anxiety, and emotional detachment, in the sense of "belle indifférence", was observed in two patients only. The cases diagnosed as mixed neurosis generally had long-standing or recurrent difficulties with various hysterical and anxious symptoms. There was one obsessional state, one psychasthenic personality (Schneider, 1950) and one patient who wished to be treated for his homosexuality. The patients in this category have very often expressed dissatisfaction with their life circumstances and in certain cases have adopted a demanding attitude toward the receiving country. Several took active steps for overseas migration, and a few intended to return to Hungary.

The organic group was too small for any generalization and the symptomatology of these cases appeared indistinguishable from English patients with similar diagnoses.

In the majority of cases, the assessment of the level of *intelligence* was based on clinical impression, taking into account the patient's educational and occupational record. Where low intelligence (I.Q.$<$85) was suspected, confirmation was always sought by testing with the Progressive Matrices of Raven. In our group we found 14 patients of low, 54 of average and 14 of superior intelligence.

The *treatment* of these cases was on the usual lines, depending on the diagnosis. Nearly half of the patients were admitted to hospital at some stage of their illness: 31·6 per cent. to mental hospitals (or observation wards) and 14·6 per cent. were referred for psychiatric opinion at a time when they were in-patients in a general hospital. A small proportion of the other cases were seen for a single diagnostic interview, and the majority were treated for varying periods as out-patients. It is not possible to make any general statement about course and prognosis, as many cases are too recent and systematic follow-up was not carried out. At least three of the schizophrenic patients have failed to respond to treatment, or have soon relapsed, and are in danger of becoming chronic cases.

Discussion

In respect of their mode of arrival in this country and their age distribution, the composition of the group of Hungarian patients here reviewed was roughly comparable to the pool of Hungarian refugees admitted to Britain since the Hungarian uprising of October 1956. For other data (Table I) comparison with the parent population is not possible as relevant figures have not yet been published, but their distribution with regard to religion, education and social class is probably similar. The incidence of broken marriages was four and one-half times higher than in non-Hungarian patients seen at the same hospital (Blacker, 1958).

The mental hospital admission rate for schizophrenic disorders is very considerably higher in immigrants than in the native population (Ødegaard, 1932; Murphy, 1955; Malzberg and Lee, 1956). A more discretely raised admission rate of immigrants has been reported for depression (Roberts and Myers, 1954; Murphy, 1955) and for organic psychiatric illness (Ødegaard, 1932; Roberts and Myers, 1954). The method of this investigation precludes any quantitative estimate of inception or prevalence rates of mental illness among Hungarian refugees in Britain.

The history of certain or probable previous mental illness in fifty per cent of our cases is similar to the 45 per cent. reported by Pfister (1955) for refugees suffering from endogenous psychoses. A disproportionately high suicide rate among refugees has been repeatedly observed (Ruesch, Jacobson and Loeb, 1948; Murphy, 1955; Pfister, 1955). Two of our patients have made very determined but unsuccessful suicidal attempts.

The frequent initial somatic presentation of mental disorder in our patients was probably culturally determined in the sense that illness was acceptable—and compatible with self-esteem—only if it occurred in the physical sphere. The language barrier, forcing designation of the complaint in concrete terms and in accordance with the patient's conception of the doctor's role, may well have been a contributory factor. The process is probably part of the "universal tendency for somatic representation of experience, converting it into action" (Lewis, 1956).

Paranoid states have been described in people finding themselves in total linguistic isolation, resolving spontaneously when verbal communication is again established. In view of the peculiar position of the Hungarian language, it may be more than a coincidence that several of the originally described cases were Hungarian speaking (Allers, 1920; Herschmann, 1921; Knigge, 1935). No such case has been observed in this series, but one patient presented a clinical picture and course similar to the closely related "primary paranoid state" (Schneider, 1930; Kino, 1951). These are characterized by strong emotional upset, florid delusions and rapid recovery, in people travelling through linguistically alien territory. Reasoning on psychological lines, the social and linguistic isolation of these Hungarian refugees would seem eminently favourable to the development of paranoid thinking (Cameron and Margaret, 1951). These probably facilitate normal projective mechanisms (Mayer-Gross, 1950) and thus could help to bring about the "paranoid" atmosphere of refugee camps (Penrose, 1952). Whether they could create, *de novo* as it were, a true paranoid delusion seems much more doubtful. In the majority of our schizophrenic patients this mechanism did not appear to play an important part, and the examination of their life history prior to emigration showed a distinctive pattern indicating an association between migratory record and this form of mental illness (Mezey, 1959).

The majority of cases diagnosed as abnormal, or psychopathic, personalities, were referred in the first six months following the arrival of the refugees to Britain, during a period when they were mostly living in hostels, often hastily improvised for this purpose. It was only to be expected that those whose social adaptation was at best fragile, should show various signs of disordered behaviour and cause further difficulties. Hysterical cases were relatively numerous; motor and sensory symptoms were seen in typical form and with a frequency not commonly met at present in British patients. This is in accordance with Eitinger's (1958) experience; he reported conversion symptoms in nearly half the psychiatric cases among refugees in Norway. The high incidence of this form of mental disorder is probably culturally determined (Harvey, 1956; Wittkower and Fried, 1958). Many of our hysterical patients had other neurotic symptoms as well and the choice of the exact diagnostic subgroup often proved an arbitrary decision. This can be related to war-time military practice, when a combination of anxiety and hysterical symptoms was seen much more frequently than either in isolation (Mayer-Gross, Slater and Roth, 1954).

SUMMARY

Clinical observations in 82 consecutive cases of psychiatric disorder in Hungarian refugees seen at the Maudsley Hospital during a two-year period are reported. The symptoms, diagnosis and treatment of these cases is described and the psychopathology discussed.

ACKNOWLEDGMENTS

I am indebted to Dr. D. L. Davies, Dean of the Institute of Psychiatry, who has made this investigation possible at the Maudsley Hospital. I should also like to thank Mr. E. Heimler, of the Middlesex County Council, Mr. E. Myers, of the Maudsley Hospital, Miss E. Pilbrow, of the British Council for Aid to Refugees, and Mrs. B. Soldi, of the National Association for Mental Health, for psychiatric social work with these patients, and Mrs. T. A. Maxwell for secretarial assistance.

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THE EFFECTS OF ELECTRIC CONVULSIVE TREATMENTS ON NITROGEN, CALCIUM, AND PHOSPHORUS METABOLISM IN PSYCHIATRIC PATIENTS

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INTRODUCTION

THIS investigation was designed to determine whether significant alterations in the metabolism of nitrogen, calcium, and phosphorus occur in psychiatric patients during the therapeutic administration of electric convulsive treatments. Gour and Chaudhry (1) observed transient changes in serum calcium following grand mal convulsions in a series of patients. Jarvie and Mulligan (2), repeating this experiment in patients receiving muscular relaxants during the administration of E.C.T., failed to demonstrate similar calcium changes. More intimate knowledge of electrolyte metabolism can be obtained by means of balance techniques (3), whereby the degree of retention or loss of a particular substance can be ascertained by maintaining each patient on a constant daily intake and regularly determining the urinary and stool excretion of that substance.

METHOD

Selected psychiatric patients, with no evidence of organic disease, were placed on the metabolic unit of the Payne Whitney Clinic preparatory to the administration of a series of electric convulsive treatments as part of their total therapy programme. Each patient was placed on a constant diet, regulating the daily intake of nitrogen, calcium, phosphorus, and other essential constituents. Twenty-four hour urine and complete stool collections were done, and analysed by standard laboratory methods for nitrogen and electrolytes. Creatinine determinations were done to insure accurate specimen collections. Following 2 control periods of approximately 9 days each, electric convulsive treatments were administered at the rate of 2 a week for 3–5 weeks.

The psychopathologic state of each patient was observed throughout the study by individual psychotherapists, psychiatrists participating in the research programme, and the psychiatric nursing staff, utilizing the special behaviour graphs described by Kohl (4). Those psychopathologic features which were most prominent in these patients included: depression of mood, paranoid features, pathologic anxiety and hostility, and hypochondriasis. Depression of mood was considered present when the patient described his state in such terms as, "sadness, hopelessness, or futility", or when his appearance, behaviour, or verbal productions revealed a depressive mood state even if he were not directly aware of it. Paranoid features were considered present when the patient revealed marked suspiciousness of the environment, ideas of reference, or frank delusions. Pathologic anxiety was recognized by subjective or objective evidence of "apprehension", with or without associated manifestations of agitation, interrupted sleep, elevated pulse rate, or autonomic nervous system involvement. Pathologic hostility was considered present when the patient, consciously and in an outward direction, manifested anger or resentment. Hypochondriasis was recognized by unrealistic over-concern about health and was usually associated with anxiety. Unconscious factors, which could be detected from the psychodynamic understanding of each patient, were not included in the psychopathologic evaluations. The attempt to describe degrees of each pathologic feature was limited to 3 categories: (1) absent; (2) present to a mild or transitory extent, indicated on the following graphs as a hatched bar; (3) present in a marked and persistent manner, indicated by a solid bar.

OBSERVATIONS

We have completed these investigations on 7 patients. Fifty-four grand mal convulsions were given in all. In none did any well-defined changes in urinary nitrogen, calcium, or phosphorus occur during the 24-hour period following each convulsion. In several patients daily urines were fractionated into 8-hour periods, but here again no significant changes could be noted on the day of each treatment.

However, when the metabolic changes occurring during the entire series of 6–10 treatments in each patient were evaluated as a whole, certain definite trends appeared. Moderate fluctuations in nitrogen and phosphorus metabolism were occasionally seen, but the most striking changes occurred in the metabolism of calcium. On the basis of calcium loss or retention, these 7 patients may be divided into 2 major groups: first, those who demonstrated a decrease in urinary calcium and an increase in calcium retention during the period of clinical improvement associated with the convulsions; and secondly, those in whom no change in calcium metabolism was observed throughout the study.

Group I: Calcium Changes Observed During E.C.T.

1. The first patient was a 34-year old woman, diagnosed as a schizophrenic reaction, paranoid type, presenting a 10-month history of severe depression of mood, paranoid delusions, resentment, bewilderment, and withdrawal. Her condition was essentially unchanged after 5 months of psychotherapy in the hospital.

Psychopathologic and metabolic observations are summarized in Graph 1. She received 8 electric convulsive treatments. Following her second treatment, in metabolic period 3, a striking disappearance of resentment and bewilderment occurred, with a reduction in depression of mood. Following E.C.T. 4, in metabolic period 4, depression of mood cleared entirely.

During control periods 1 and 2, her average urinary nitrogen ranged from 11·38 to 12·38 g. daily, with a balance ranging from a loss of ·79 to a retention of ·58 g. daily. The average daily urinary excretion of calcium ranged from ·228 to ·231 g., with overall calcium retention ranging from ·022 to ·192 g. daily. The average daily urinary phosphorus ranged from ·846 to ·886 g. daily, the total balance varying from a loss of ·092 to a retention of ·050 g. daily. These 2 periods may be considered essentially comparable.

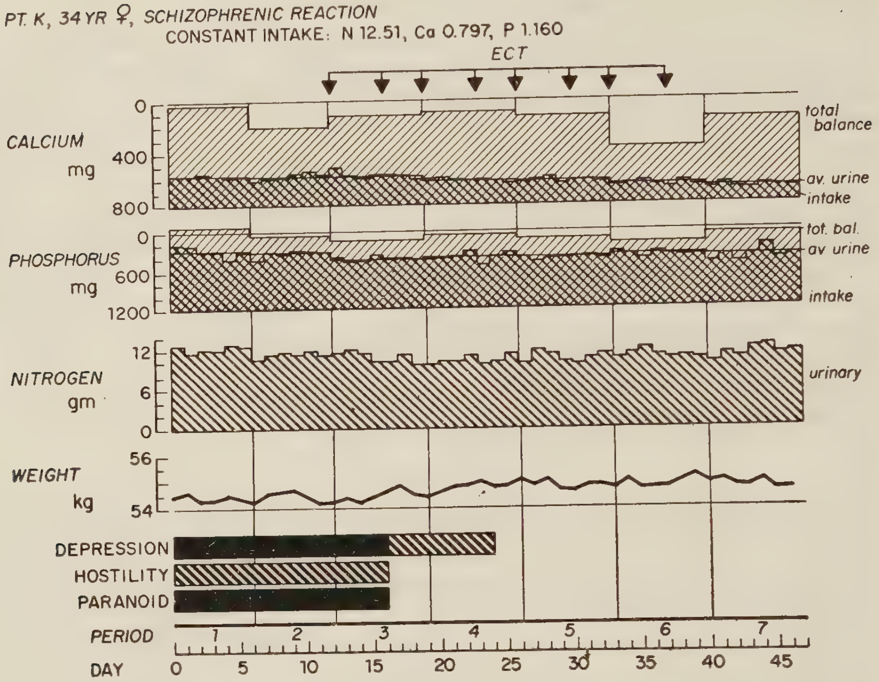

Fig. 1

Throughout the entire study, the patient remained in slightly positive nitrogen balance, with a slight decrease in urinary nitrogen occurring during periods 3, 4, and 5. Her phosphorus balance did not change significantly, but a slight reduction in urinary phosphorus was noted during period 3, reaching an average excretion level of ·747 g. daily and remaining at that level throughout the rest of her course.

Except for a slight increase in urinary calcium on the day of the first convulsion, her average urinary loss of calcium was unchanged in period 3. In period 4, however, reduction in urinary calcium was noted, the daily excretion averaging ·188 g. Her urinary calcium continued at about the same level in period 5, averaging ·177 g. daily. During period 6, urinary calcium excretion was reduced further to an average level of ·149 g. daily. In period 7, an even lower level was noted, ·127 g. daily.

This patient remained in moderately positive, essentially unchanged calcium balance until period 6. At that time a marked increase in calcium retention was observed, the patient retaining ·369 g. daily. This change was temporary, and during period 7 she again returned to a more moderate calcium retention of ·147 g. daily.

2. The second patient was a 41-year old woman, diagnosed as a depressive reaction of middle life, presenting a 1-year history of fears of being alone at night, of being sexually molested, or of appearing in crowded places. For 1 month she had difficulty falling asleep, angry outbursts and paranoid delusions of being accused of communism, with marked depression of mood. Her condition was essentially unchanged during 3 months of psychotherapy in the hospital prior to study. On the metabolic unit she received 6 electric convulsive

treatments, improving markedly after the second and with complete disappearance of symptoms following the fourth. Her weight remained constant throughout.

The patient was placed on a constant diet, containing 12·90 g. of nitrogen, ·940 g. of calcium, and 1·275 g. of phosphorus. During control periods she retained 2·06 g. of nitrogen daily, with a urinary excretion averaging 9·96 g. daily. She retained ·138 g. of phosphorus daily, with an average daily urinary loss of ·752 g. Her calcium retention was ·180 g. daily, with a urinary calcium excretion averaging ·132 g. daily.

No significant changes in nitrogen or phosphorus metabolism were noted throughout the administration of the series of electric convulsive treatments. During metabolic period 3, associated with the administration of E.C.T. 1 and 2, no significant alteration in calcium metabolism occurred. During period 4, corresponding to E.C.T. 3 and 4, an increase in calcium retention was noted to the level of ·246 g. daily, but with no change in urinary excretion. By this time a significant clinical improvement had occurred. During metabolic period 5, associated with E.C.T. 5 and 6, calcium retention increased somewhat further to ·299 g. daily, with a decrease in average urinary calcium excretion to ·115 g. daily. During the post-treatment period her calcium retention returned to its control level of ·194 g. daily, but a further slight decrease in urinary calcium to a daily level of ·106 g. was noted.

3. The third patient was a 57-year old woman, diagnosed as a depressive reaction of middle life, presenting a 7-month history of depression of mood, early morning awakening, strong feelings of guilt and loneliness, and a loss of interest in usual activities. Metabolic studies were initiated at the time of her admission to the hospital, and a slight improvement in her overall condition occurred before the initiation of electric convulsive treatment. She received 9 E.C.T., the first 3 of which failed to induce grand mal convulsions. In association with the first 4 E.C.T., anxiety, resentment, and depression of mood increased somewhat. During the metabolic period corresponding to E.C.T. 5, 6, 7, 8, and 9, a definite reduction in anxiety, resentment, and depression of mood was noted, but a substantial improvement in her psychopathologic state did not occur until the week following the end of treatments.

During the studies her weight fell from 59 to 54 kilograms, in spite of the fact that she was being maintained on a constant diet, containing 12·45 g. of nitrogen, ·803 g. of calcium, and 1·206 g. of phosphorus. During the control periods she retained ·180 g. of nitrogen daily, with an average urinary excretion of 11·12 g. She retained ·184 g. of calcium, with an average urinary excretion of ·138 g. She retained ·072 g. of phosphorus, with an average urinary excretion of ·831 g.

No significant changes in the metabolism of nitrogen, calcium, or phosphorus were noted during the metabolic period corresponding to the first 4 electric convulsive treatments. During the period corresponding to E.C.T. 5 through 9, a slight increase in urinary calcium was noted, rising to a daily average level of ·162 g., but associated with a substantial increase in calcium retention to a level of ·301 g. daily. No significant changes in nitrogen or phosphorus were seen.

During the periods of study following treatment, her nitrogen balance became slightly negative, the patient losing ·42 g. daily, with an average urinary excretion of 11·64 g. At the same time her weight decreased sharply. Her calcium balance returned to a retention level of ·150 g. daily, and her urinary calcium dropped to ·095 g. Phosphorus metabolism was essentially unchanged.

4. The fourth patient was a 50-year old woman, diagnosed as a middle life depressive reaction, presenting an 18-month history of depression of mood, pathologic resentment and suspiciousness, insomnia, and anorexia. No essential change in her clinical state occurred during the 4 months of psychotherapy in the hospital prior to metabolic studies. The psychopathologic and metabolic observations on this patient have been summarized in Graph 2. In order to clarify the nature of the calcium changes observed in the preceding 3 patients, this patient was placed on a constant diet deficient in calcium, thereby accounting for the strongly negative calcium balance in the control periods. An intravenous calcium tolerance test was done between metabolic periods 3 and 4, and the patient demonstrated increased urinary calcium and temporary suppression of urinary phosphorus, similar to that seen in normals on the day of the tolerance test (5). Immediately following the calcium tolerance test, however, a distinct change in her mental state occurred, characterized by the disappearance of suspiciousness and a decrease in resentment, with greater alertness to her environment and less external evidence of depression. However, no change in her basic mood of "hopelessness" was seen.

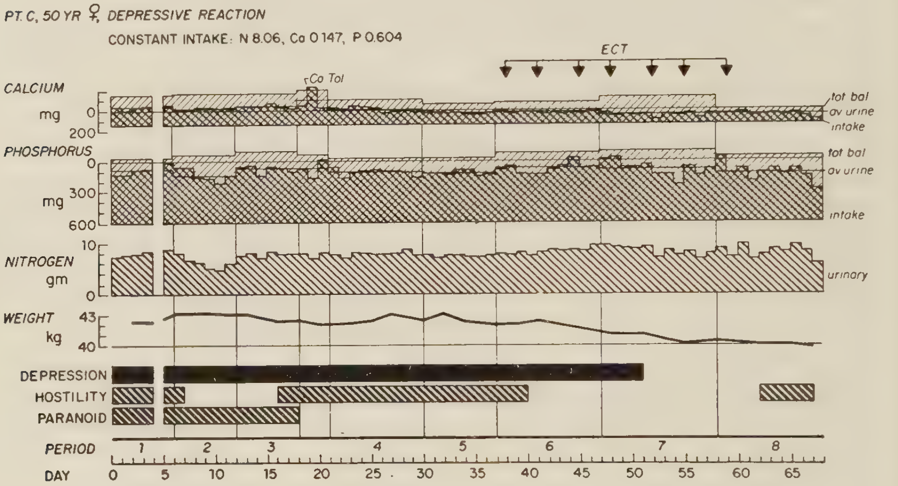

FIG. 2

The patient was given 7 electric convulsive treatments modified by the use of anectine, a muscular relaxant, and pentothal anaesthesia. In metabolic period 6, following the second treatment, resentment was no longer evident. During metabolic period 7, following the fourth treatment, her depression cleared entirely.

During the first 3 control periods, slight fluctuations in nitrogen and phosphorus metabolism were noted, but urinary calcium and calcium balances remained relatively constant. In periods 1 and 3 she was in a slightly negative nitrogen balance, losing ·41–·54 g. daily. Her average urinary nitrogen excretion ranged from 7·78 to 7·99 g. daily. During metabolic period 2, however, she retained 1·16 g. of nitrogen daily, and her average urinary loss fell to 6·06 g. daily. Her phosphorus balance was essentially comparable in all

3 periods, the patient's loss ranging from ·030 to ·097 g. daily. During metabolic periods 1 and 3 her urinary phosphorus ranged from an average of ·516 to ·526 g. daily, but during control period 2 a decrease to an average daily loss of ·452 was observed. During all 3 periods her negative calcium balance ranged from ·140 to ·163 g. daily. Her urinary calcium excretion ranged from ·166 to ·186 g. daily, essentially comparable, but perhaps slightly elevated considering the low intake of calcium.

No significant changes in nitrogen or phosphorus metabolism were noted during control periods 4 and 5. A slight, but probably not significant decrease in calcium loss was observed, so that in period 5 her negative balance amounted to only ·053 g. daily. Urinary calcium decreased to an average daily level of ·119 g. in period 5.

During metabolic period 6, associated with the first 3 E.C.T., her negative nitrogen balance increased slightly to a loss of 1·10 g. daily, with a rise in average urinary nitrogen excretion to 8·23 g. daily. Calcium and phosphorus balances were essentially unchanged. Her average urinary calcium excretion remained at a level of ·119 g. daily, but her urinary phosphorus excretion rose somewhat toward the end of the period, giving her an average daily loss of ·524 g. During period 7 she received E.C.T. 4, 5 and 6. Her nitrogen loss was essentially comparable to that of period 6. Her phosphorus balance was unchanged, but her urinary phosphorus excretion averaged ·512 g. daily, this figure representing a high of ·630 g. at the beginning of the metabolic period and a low of ·358 g. late in the metabolic period. Her negative calcium balance increased slightly, the daily loss amounting to ·110 g. However, urinary calcium was further reduced to an average excretion of ·095 g. daily. A loss of nearly 3 kg. in weight occurred during these two periods.

The seventh and last treatment was given in metabolic period 8. Her negative nitrogen balance was reduced slightly, as was the average daily urinary excretion of nitrogen. The negative phosphorus balance continued, amounting to ·032 g. daily, with an average urinary loss of ·479 g. daily. She was essentially in calcium balance. Her urinary calcium excretion remained at a low level, averaging ·096 g. daily.

Group II: No Calcium Changes Observed During E.C.T.

1. The first patient was a 55-year-old woman, diagnosed as a depressive reaction of middle life, presenting a 5-month history of anxiety, with marked tearfulness, insomnia, and fear of being alone. During 4 months of psychotherapy in the hospital prior to study her clinical state fluctuated somewhat, but she persistently denied feeling depressed, describing chiefly anxiety. Her pulse was elevated to a range of 90–100 per minute, with occasional spiking to 120. On the metabolic unit, she received 9 electric convulsive treatments, associated with an increase in anxiety, marked fear of losing her memory, mild confusional changes, and many vague somatic complaints. No clinical improvement was noted until 2 weeks following the final treatment, at which time she seemed somewhat less anxious and depressed.

Psychopathologic and metabolic observations have been summarized in Graph 3. No change in depression of mood was noted during the entire course of treatment. Moreover, following the administration of the first treatment, anxiety and hostility were actually intensified.

In control periods 1 and 2 she was in a slightly negative nitrogen balance, ranging from ·35 to ·97 g. daily. Her urinary nitrogen excretion was constant, averaging 12·00 g. daily. She retained ·259 g. of calcium in period 1, and ·069 g. in period 2. Urinary calcium ranged from ·117 g. daily in period 1 to ·096 g. in period 2. She retained ·103 g. of phosphorus in period 1, lost ·129 g. of phosphorus in period 2. Her average urinary excretion of phosphorus ranged from ·691 to ·716 g. daily in the control periods. The decrease in calcium and phosphorus retention observed in period 2 probably represents a technical error in stool division.

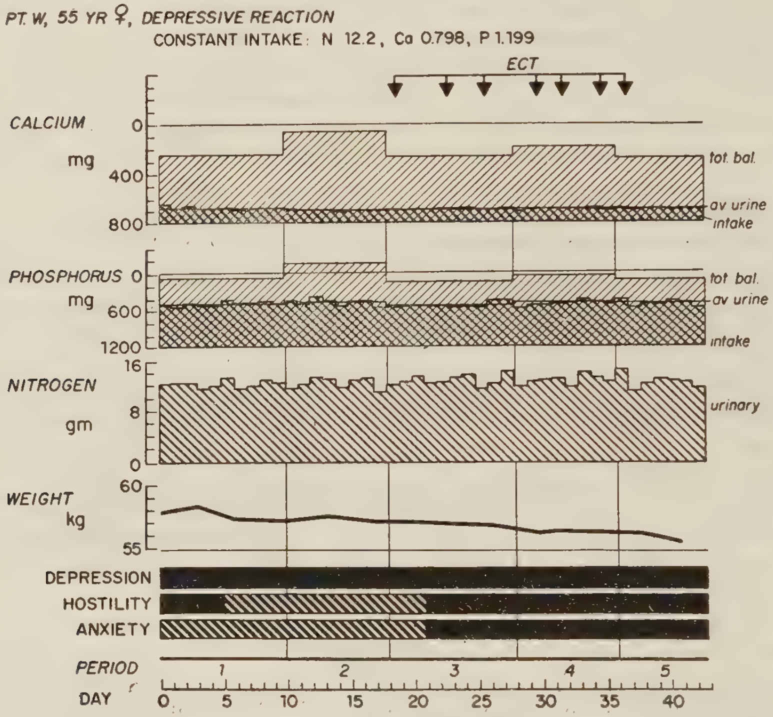

FIG. 3

During metabolic periods 3, 4, and 5 the patient continued in a negative nitrogen balance, losing from ·56 to 1·10 g. daily, with an average urinary nitrogen excretion ranging from 12·07 to 12·41 g. daily. Simultaneously she lost nearly 3 kg. in weight.

During periods 3, 4, and 5 she retained ·057 to ·137 g. of phosphorus daily, with an average urinary loss ranging from ·659 to ·694 g. daily. At the same time her calcium retention ranged from ·194 to ·298 g. daily, with an average urinary calcium loss remaining remarkably stable at ·101 g. daily. In essence, this patient showed no immediate improvement during E.C.T., and no significant changes in nitrogen, calcium, or phosphorus metabolism occurred during the series of convulsions.

2. The second patient was a 36-year-old man, diagnosed as a schizophrenic reaction, paranoid in type, presenting a 7-year history of insidious withdrawal, apathy, anxiety and discouragement, with transient ideas of reference, and pathologic resentment. His condition remained essentially unchanged during the 5 months of psychotherapy in the hospital prior to study. On the metabolic unit he received 10 electric convulsive treatments. A definite, but limited

decrease in anxiety, resentment, apathy, and depression was noted following the second E.C.T. However, in spite of continued treatments, no further improvement was observed, and a temporary marked memory difficulty appeared following the eighth treatment.

He was maintained on a constant diet, receiving 14·60 g. of nitrogen, 1·071 g. of calcium, and 1·646 g. of phosphorus daily. His weight remained stable throughout. During control studies he was in slightly negative nitrogen balance, losing ·76 g. daily, with an average urinary excretion of 14·62 g. His calcium balance was positive, with a retention of ·135 g. daily, and an average urinary excretion of ·099 g. He retained an average of ·012 g. of phosphorus daily, with an average urinary excretion of 1·126 g.

Associated with the first two E.C.T., a shift in nitrogen balance to retention occurred, amounting to ·57 g. daily, with a decrease in the average daily urinary nitrogen excretion to 13·57 g. A marked increase in calcium retention to a level of ·443 g. daily was observed, but there is laboratory evidence that this change reflected a technical error in stool division. Urinary calcium rose slightly to ·110 g. daily. Phosphorus retention increased to ·138 g., with no change in urinary phosphorus excretion. During the subsequent 8 electric convulsive treatments, nitrogen retention increased, reaching a high of 1·16 g. daily in association with E.C.T. 9 and 10. Urinary nitrogen was essentially constant. Calcium retention varied from ·132 to ·177 g. daily, and the average daily urinary calcium excretion, after reaching a high of ·121 g. at the time of E.C.T. 7 and 8, again fell to the control level of ·094 g. daily. Phosphorus retention ranged from a low of ·052 g. to a high of ·163 g., increasing slightly above control values. The average urinary excretion of phosphorus decreased to a low of ·938 g., associated with E.C.T. 5, 6, 7, and 8, and rising to the pre-treatment control level thereafter.

3. The third patient was a 48-year-old man, diagnosed as a depressive reaction of middle life, presenting a 12-year history of anxiety, with strong recurrent, unfounded fears of cancer. Three weeks before hospitalization, anxiety increased markedly, with insomnia and depression of mood. During 2 months of psychotherapy in the hospital prior to study, his hypochondriacal overconcern, hopeless mood, and agitation continued unabated.

The psychopathologic and metabolic observations are summarized in Graph 4. In order to clarify the nature of calcium changes which might occur, he too was placed on a diet deficient in calcium. He received 8 electric convulsive treatments, modified by the use of anectine and pentothal anaesthesia. These resulted in no relief from anxiety, but a definite decrease in depression following the fifth treatment. Episodes of resentment continued throughout the study.

During control periods 1 and 2, on a constant calcium-deficient diet, the patient was in a negative nitrogen balance ranging from 2·40 to 3·17 g. daily, with average urinary excretion ranging from 9·69 to 10·70 g. daily. The negative phosphorus balance ranged from ·151 to ·212 g., with a urinary excretion of ·580 to ·599 g. daily. The negative calcium balance ranged from ·083 to ·139 g. daily, with a urinary excretion of ·116 g. daily.

Throughout the administration of the electric convulsive treatments, his nitrogen balance remained strongly negative, ranging from 2·17 to 3·44 g. daily, the highest loss being reached in period 6 at which time E.C.T. 7 and 8 were given. Urinary nitrogen excretion averaged 9·14 to 10·64 g. daily, essentially unchanged. He lost nearly 5 kg. in weight throughout the study. Phosphorus balances remained negative, ranging from ·150 to ·281 g. daily,

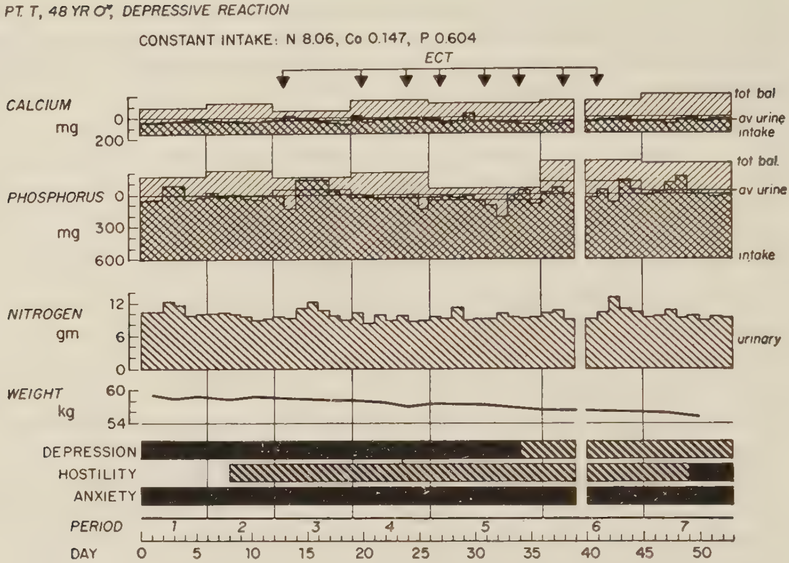

Fig. 4

except during period 5. At that time, in association with E.C.T. 4, 5, and 6, his phosphorus loss was insignificant. Urinary phosphorus ranged from ·542 to ·706 g. daily, reaching a low in period 5 and a high in period 6. In metabolic period 5, urinary phosphorus ranged from a low of ·389 following E.C.T. 5 to a high of ·626 following E.C.T. 6.

His calcium balances remained negative throughout, ranging from a low of ·064 g. in period 3 to a high of ·214 g. in period 7. Urinary calcium excretion remained remarkably unchanged throughout, with the average daily values ranging from ·109 to ·125 g. daily.

Discussion

In this series of 7 patients studied during the administration of electric convulsive treatments, no changes in nitrogen, calcium, or phosphorus metabolism were observed during the 8 to 24-hour period following each grand mal seizure. This is particularly interesting in view of the intense physiologic stress to which each patient was repeatedly exposed during the treatments. Naturally, it is possible that changes in these electrolytes do occur, but are too limited in time to be detected by balance methods.

Depression of mood constitutes one of the leading psychopathologic indications for the use of electric convulsive treatments. However, in order to produce the desirable clinical effects, at least 3 or 4 convulsions usually must be given. In order to sustain the clinical improvement, at least 6 to 10 treatments must be given. It is therefore conceivable that biological changes accompanying the psychological improvement may be associated with the entire series of convulsions rather than with individual treatments. In 4 of the patients studied here, a reduction in urinary calcium excretion and an increase in overall calcium retention were observed during the series of electric convulsive treatments. In 3 of the patients no such changes were noted. No well-defined relationship was apparent between calcium changes and age, sex, or menstrual status of the patients, or the use of muscular relaxants to modify the treatments. Interestingly, the 4 patients with calcium changes also experienced the most striking degree of clinical improvement as a result of treatments. Moreover, their depressed states were characterized by the initial presence of pathologic hostility and paranoid features. Those 3 depressed patients with no calcium changes showed much slower, more limited clinical improvement and demonstrated, during the control studies, additional features of pathologic anxiety and hypochondriasis. It is impossible to state, on the basis of these few patients, whether the differences in associated psychopathologic features are in any way related to the differences in their metabolic responses to electric convulsive treatments. However, these observations do suggest that in certain depressed states abnormalities in calcium metabolism or in those bodily mechanisms which affect calcium metabolism may be involved. For instance, disorders of the parathyroid gland are often associated with personality changes characterized by tension, irritability, and depression of mood; and Richter (6) was successful in alleviating recurrent depressive episodes in a patient with hypoparathyroidism by the administration of calcium and AT-10. It remains to be clarified whether the calcium changes which we have observed are of fundamental importance or serve to mirror other biological processes which may be activated, such as alterations in endocrine function.

SUMMARY

Electric convulsive treatments were therapeutically administered to 7 psychiatric patients. Two patients were diagnosed as schizophrenic reactions, 5 as depressive mood disorders. Complete balance studies were done on the metabolic unit of the Payne Whitney Clinic before, during, and after the series of treatments. Determinations of nitrogen, calcium, and phosphorus excretion were done. Four patients demonstrated a gradual, progressive decrease in urinary and stool calcium loss, with an associated increase in calcium retention during the administration of electric convulsive treatments. Three patients showed no alteration in calcium metabolism. This experiment revealed no significant changes in nitrogen or phosphorus excretion. In those patients demonstrating calcium retention, the metabolic changes did not appear related to individual electric convulsive treatments, but rather to the overall series of 6–10 treatments. Moreover, these same patients demonstrated a more striking degree of clinical improvement than those in whom no calcium changes were noted.

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AUTOBIOGRAPHIES OF FORMER MENTAL PATIENTS*

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MANY years ago one of us was introduced by a senior colleague to Thomas Hennell's fine book, *The Witnesses* (23), and so began in a desultory way to collect accounts of their illnesses written by mentally ill people. We have found that many people know a few books of this genre and speak warmly about their usefulness. One gets the impression that these books are unobtainable. In 1956, after reading Hunter's and MacAlpine's (44) translation of the Schreber *Memoirs*, and later *Schizophrenia, 1677* by the same authors, which consists of Haitzman's account of his illness, we realized that these books had played and could play an important part in the development of psychiatric theory. Indeed, the psychoanalytic theory of schizophrenia derives from the Schreber *Memoirs* and, although Hunter and MacAlpine rebuke Freud for his extremely selective use of those memoirs, they do not suggest that any systematic study of these writings would be valuable. Psychiatrists of many different persuasions have been given to examining a host of historical, literary, and mythical characters from Moses to Popeye the Sailor; but so far we have been unable to find any systematic study of this uniquely valuable body of information provided by the sick themselves.

In these books, then, the mentally ill have given their own views about their illnesses and on the way in which they were treated. We are often so concerned with the motives and dynamics of our patients that we pay little attention to what they themselves say about their illnesses and what they believed helped or hindered them in their struggle to get well. In so far as we accept the evidence which they give, it has been with condescension and never as experts whose appalling adventures might enlarge our understanding and help us to benefit other sick people.

Why has this happened? Most important perhaps is the fact that very few psychiatrists or psychologists are aware that there is a substantial body of available data which needs to be examined†. Classics like *A Mind that Found Itself* (12) are so well known that equally valuable books are neglected. It may also be that we are unwilling to subject ourselves to the tiresome vapourings of paranoid and disgruntled people whose embittered stories would not, we feel, be typical. In this paper we hope to show that this fear is unjustified and that

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* The study was supported by grants from the Rockefeller Foundation and the Department of Health and Welfare, Ottawa. Gwyneth Witney and Dorothy Sommer read many of the books and helped prepare abstracts. A number of colleagues helped locate individual autobiographies: Dr. J. D. Griffin, Paul Harris, William Moore.

† This is also true in regard to accounts by former inmates of concentration camps. It was not until we had read a summary article by a sociologist (4) that we learned that over a hundred of these books are in print.

for every book which seems over-critical there is another which errs on the side of panglossian optimism. These books are remarkably well-written, and their readers are seldom bored. These authors are the insiders of mental hospitals, and we as outsiders have been reluctant to believe that they might have anything useful to contribute. Yet what other source of information is so uncontaminated by our professional influence? It is easy for us to become extremely ignorant of things that go on under our noses, and, although a proportion of the many thousands of psychiatrists and psychologists in the world must become patients in mental hospitals every year, unfortunately they rarely write about their experiences; and even if they did, it is unlikely that these would be typical. When Caudill lived on a ward for some time and described its life, he found himself accused of "going patient" and "losing his objectivity". It is almost as if we really did not want to hear our patients' opinions of the care we provide. This is a not uncommon medical attitude. It is understandable that we should wish to insulate against our patients' anguish so that we can get on with the job of bettering them. Yet one wonders whether, particularly in psychiatry, we can afford the continued luxury of this ignorance. D. O. Hebb, commenting on Senden's monograph about the congenitally blind people who regained their sight, writes:

> Senden's monograph is a compilation of all published reports on the vision of the congenitally blind given sight by a surgical operation after the patient was old enough to talk to the examiner and describe what he saw. In some respects the data are incomplete, but the report is repeatedly referred to here because it contains the only existent evidence concerning the course taken by the early development of human perception. At first sight, some of the reported facts are literally almost incredible, since they differ so much from what would be predicted by current theory. There is, however, a considerable unanimity among the writers reviewed by Senden, some of whom evidently were not aware of the reports made by others (6, p. 18).

We believe that these records of mentally ill people properly used can provide us with equally surprising information. They are a body of data which can be examined by people who are geographically removed from each other, and they can be added to in an orderly way. By comparing them with accounts written in other languages and by other generations, we can learn more about the effects of history and culture upon mental illness. While these books are clearly the work of literate and intelligent people and so are an atypical sample of the mentally ill, they cover a wide range of illness, age, and occupation. They have rarely been screened by medical men and have not been written to illustrate any particular psychiatric hypothesis. We hope to show in this and other papers some of the possibilities of these remarkable works and encourage others to use them too.

METHOD

The first problem was to establish criteria which would provide a sample with certain common and objective characteristics. This was important because it guided us in finding suitable material and will allow others to repeat our study. While such criteria may sometimes exclude useful accounts, they are essential if generalizations are to be made from the data.

After we had read many of the books and had had many discussions, we decided to exclude:

1. Fiction.
2. Accounts by other people such as therapist or friend unless he acts solely as scribe.

3. Descriptions of illness without hospitalization.
4. Autobiographies in which the illness forms only a small and unimportant part of the story.
5. Brief articles and unpublished manuscripts.
6. Narratives not translated into English.

All the books in our sample meet the following criteria:

1. The author was or had been a patient in a mental hospital.
2. The book was frankly autobiographical.
3. The book was devoted primarily to a description of mental illness or mental hospitals.

These criteria were adopted so as to simplify the task of selection and make it more objective. For example, restricting our sample to frank autobiographies made it unnecessary to decide whether a realistic novel was or was not "genuine". Excluding articles saved us from a plethora of stories from sensational magazines and popular weeklies. Although there were some unhappy applications of these criteria, we feel that the study could not have been carried out without a few casualities among the many biographies, autobiographies, and novels of mentally ill people. *The Maniac* and *Schizophrenia 1677*, two classics, were lost to us because the authors never entered hospital. *The Snakepit* and *Shutter of Snow*, among others, were rejected as fiction. Cocteau's *Opium* and *Anastasia* devoted too little space to mental illness to add materially to the study.

There are also several newsletters edited by former mental patients that provide a wealth of information on hospitals and psychiatry. Two of these publishing at the present time are *Search* and *The Cross*. The former is devoted largely to news of ex-patient clubs and activities and gives some excellent accounts of how clubs are formed and why they fail. *The Cross* is a frankly crusading venture, edited by a lawyer, and contains news of court cases and litigation involving mental patients. The editors of both periodicals are included in our sample of ex-patient authors as each has written an account of his experiences. The newsletters contain vivid descriptions of hospital life by former patients and are worth consulting for this material alone. We have not used any of these narratives in our sample, as they are not generally available and are brief.

Applying these criteria to the books we had collected left thirty-seven autobiographies. Ultimately we hope to use the excluded accounts for other studies in which different selection methods will be employed. In this paper we shall make a general survey of published autobiographies of former mental patients. We will not attempt to explore in any detail their *Umwelt* or life-space.

Our first task was to discover books of this type and obtain their titles, our next to get copies of the books which were often out of print. The titles were located in a variety of ways. We learned about the largest number from colleagues who had previously read them. The next best source was a group of second-hand booksellers who were contacted by mail. They put us on the trail of about one-fourth of the sample. Five fairly recent books were found through advertisements in various periodicals. Three were located from textbook references, two through library reference services, and two through mention in other autobiographies.

A surprising aspect of our search was the little we learned from our authors about similar books by others. If one were reading books by explorers, they would certainly mention previous expeditions into the same territory. In most studies of a special field one will find that, if he encounters two or three books, he will soon learn of related works by examining footnotes, references, and the text of the books he already has. It can be noted that these books do not lack for footnotes and a few contain bibliographies and appendices. The implications of this point will be discussed later.

Even in our rather isolated location, it was no problem to secure a book once we knew the author and title. We received at least two offers for almost all books. The median price we paid for books was five dollars. Textbooks were not particularly good sources for locating autobiographies, as most listed only one or two books with which the author was personally acquainted. The only comprehensive list of relevant books was compiled by Menninger (8). Unfortunately, it made no distinction between fiction, biography, and autobiography, so was not suited to our purposes. It also mentioned none of the nine English autobiographies included in our sample. Allport (1) in his monograph on the use of personal documents in psychology, mentions six autobiographies but does not discuss them at length.

We are certainly aware that the present list is incomplete. We hope that psychiatrists will apprise us of titles we have overlooked, and an addendum can be published later. We hope also that psychiatrists in non-English speaking countries will be encouraged to compile similar lists. It is important to learn to what extent the patient's perception of his illness and hospital life are transcultural. From the few French and German accounts we have seen, there is much greater use of private rooms and individual nurses. Delusions are fairly stable and include the familiar ones of drugged food and electric waves; however, our group of non-English autobiographies is very small.

Our experience leads us to believe that these books can be readily obtained at small cost of money or effort. We were a thousand miles from our nearest supplier of used books. This is important to know since it indicates that the autobiographies provide data that can be used by investigators and students in many places and at many times. We hope that the present paper will help preserve this rich legacy for psychiatry. There is probably no danger that classics such as *A Mind that Found Itself* and the Schreber *Memoirs* will be forgotten, but less well-known and equally perceptive accounts such as *These are My Sisters*, and *The Mind in Chains* could easily be overlooked at some future date.

All books in the sample had been read by at least two people connected with the study. This was not onerous as might be expected with the reading of thirty-seven assorted books, many by non-professional authors. We found that almost all of the books made easy reading with the devastating exception of the repetitious account by Graves which was not written for publication. The styles of writing ranged from beautiful to clumsy, with a median above the average mark. We felt that if a random selection of novels had been made, the interest value of our thirty-seven accounts would not have been exceeded. Our difficulty was not in finding people to read the autobiographies but in keeping track of our collection. Books were continually lent to friends and circulated throughout the hospital. Several people commented that this was the easiest way to learn psychiatry. Perhaps this is overstating the case somewhat, but it was apparent that our readers, lay and professional alike, considered the books to be both interesting and informative and gave them a much clearer picture of the world of the mental patient than they had previously.

Results

The final sample contained thirty-seven books; seven by alcoholics, ten by paranoid schizophrenics, seven by non-paranoid schizophrenics, ten by manic-depressives, and three by neurotics. Wherever possible we used the diagnosis given the patient by the hospital staff, whether or not the patient agreed that he had this illness. The one drug addict (King) was included in the alcoholic group. We experienced difficulty in only three cases where no staff diagnosis was mentioned and we had a choice between paranoid schizophrenia and catatonic schizophrenia. The matter was resolved through a discussion of symptoms by three people who had read each of the books.

Twenty-five of the authors were men and twelve were women. In all major diagnostic categories the number of male authors exceeded the number of female authors. When they first entered hospital, three of the authors were in their teens, eleven were in their twenties, twelve were in their thirties, seven were in their forties, and one was in his sixties. The ages of three patients could not be determined. The median age for the total sample was thirty.

In terms of total length of hospitalization, the alcoholics had a median stay of five months and a range from two months to one year. The paranoid schizophrenics averaged two years (range six weeks to nine years). The manic-depressives averaged two years, but this was a misleading figure since it is based on the sum of all hospitalizations. The average length of stay for single admissions of manic-depressives was less than a year. The non-paranoid schizophrenic group averaged one year in hospital.

Although our sample consisted mainly of short-term patients, there are several who spent many years in hospital. The longest continuous hospitalization was thirteen years (Jane Simpson) followed by nine years (Judge Schreber) and four years (Jane Hillyer). The remainder of the sample was short-stay patients but many had been ill for some time before entering hospital. Time in hospital was only one event in the author's illness and recovery. Length of stay in hospital seems a better index of social attitudes and hospital discharge policy than of duration of mental illness or efficacy of treatment. In discussing the case of Ezra Pound, Szasz (10) shows clearly that Pound's discharge bore little relation to his mental state.

Both age and illness show that this is not a representative group of hospital patients. There is an over-representation of alcoholics and paranoids and an under-representation of non-paranoid schizophrenics. There were no character disorders (except perhaps in the alcoholic group). There were no G.P.I. cases or diseases of the senium. The story of the elderly mental patient is yet to be written. Neither fictional nor personal accounts of elderly mental patients have come our way. Since 40 per cent. of beds in many mental hospitals are filled by people over sixty, this is particularly unfortunate. Of the schizophrenic group three patients describe catatonic episodes but we have no description of hebephrenia. The only account of chronic schizophrenia is provided by Hillyer. When we consider the type of ward on which the patient had stayed, the picture is not so one-sided. Excluding the alcoholics, at least one-third of the patients had spent time on long-stay or refractory wards. The majority of alcoholics had been in private hospitals at one time or another as contrasted with less than a third of the other patients.

It was very difficult to establish a social class to which the patients belonged. They seemed to be more intelligent and better schooled than well off financially. Most of them had come down in the world before entering hospital. Many entered hospital destitute whereas several years before they had been comfortably situated.

Regarding occupation, the authors, excluding the alcoholics, are a heterogeneous group. There are nine members of the professions; seven people in the practising arts (five of whom are writers); five people who held minor clerical positions; and one each in athletics, business, public relations, and club leadership, along with two housewives. The alcoholics were more homogeneous as five had been writers, with one actress and one waitress. For the total sample there is an over-representation of the professions and arts and an under-representation of blue-collar and business people. The preponderance of professional writers in a sample of authors of any kind is understandable. A person earning his living with a pen would find it difficult to resist writing about his experiences in a mental hospital. In several instances the ex-patient turned to writing after leaving the hospital. These cases, not listed as authors in the occupational summary which referred to pre-hospital vocation, were launched on literary careers by their illness and hospitalization. Several other ex-patients found scope for their energies in the mental health field. Boisen became a hospital chaplain; Beers founded the mental hygiene movement in the United States; Johnson became an ardent champion in parliament for the rights of the mentally ill; Pollitt and Moore both edit mental health newsletters; Dahl is director of a state mental health association; Roth lectured extensively for A.A.; and Maine became a well-known writer on mental health topics.

In terms of family rejection, there were four manic-depressives, four alcoholics, and two paranoid schizophrenics who were divorced or legally separated from their spouses. The picture is complicated somewhat by age differences between the groups and patients who were never married, but the trend is clear. Regardless of diagnosis, these patients have a higher divorce rate than the general population. The tenor of the books indicated greater family rejection of the alcoholics than of the other patients. From a theoretical standpoint this seems important in view of the many accounts of family rejection in schizophrenia. It is necessary to learn to what extent this relates to grievous illness *per se* rather than to a particular form of mental illness.

The chronology of these autobiographies shows that the 1950's produced a striking increase in the number of books by paranoid schizophrenics. Table I shows the original publication date of the autobiographies. Of the twenty-one books published before 1950, only two were by paranoids. Of the fifteen books published in the last decade, eight were written by paranoids.

TABLE I

Original Publication Dates of Autobiographies

Author's Illness	Before 1920	1920–1929	1930–1939	1940–1949	1950–1959
Alcoholism	0	1	3	2	1
Paranoid schizophrenia ..	1	0	1	0	8
Schizophrenia	1	0	2	2	2
Mania-depression	1	0	2	3	4
Neurosis	0	1	0	1	1

Some interesting trends emerge when the format of the books is considered. This refers only to the format of the original addition. Table II shows the number of books containing forewords written by other people. We see that none of the ten books by paranoids contained such forewords, while fourteen of the twenty-seven books by other patients did. The contrast is especially marked between paranoid schizophrenics and manic-depressives.

TABLE II

Number of Books with Forewords in Original Edition

Author's Illness	Foreword by Another Person	No Foreword or Written by Author
Alcoholism	2	5
Paranoid schizophrenia	0	10
Schizophrenia	3	4
Mania-depression	8	2
Neurosis	2	1

This trend is reversed when the number of books with appendices and epilogues is considered. The authors who use such supplementary sections are overwhelmingly in the paranoid group.

TABLE III

Number of Books with Author's Appendix, Epilogue, or Bibliography

Author's Illness	Number of Books with Supplementary Section
Alcoholism	1
Paranoid schizophrenia	7
Schizophrenia	2
Mania-depression	1
Neurosis	0

The reputation of the publisher of the first edition provides an interesting difference. Twenty-one of the twenty-six books by non-paranoid authors were published by well-known commercial firms or university presses; however, nine of the ten paranoid patients had their books published by lesser known firms. This difference is shown in Table IV.

TABLE IV

Reputation of Autobiography Publishers

Author's Illness	Well-known, Commercial	Medical or University	Little-known, Commercial
Alcoholism	4	1	2
Paranoid schizophrenia	1	0	9
Schizophrenia	4	1	2
Mania-depression	8	1	1
Neurosis	3	0	0

To show how rich these autobiographies are in material for clinical research we will touch briefly on two aspects of them. First, there are the many reports of perceptual changes which are of particular interest to psychology and psychiatry. Second, there is the comparison between mental hospital and prison life which concerns sociologists and psychiatrists. In this paper we will not discuss either of these fields in detail, but simply indicate some of the possibilities.

The books present many descriptions of perceptual changes experienced by the authors. Most mentioned illusions of various types, especially of faces and people close to them. Only eight patients, excluding alcoholics, described actual visual hallucinations. The conditions under which these occurred were remarkably similar and are reproduced in Table V. Several others mentioned auditory hallucinations but, since it was very difficult to tell when the voices were actual hallucinations and when they were ideas or thoughts, we will confine the analysis to visual phenomena. Excluded from the table are illusions (misperceptions of actual stimuli) and hypnagogic imagery. This table discloses that the majority of visual hallucinations occurred under conditions of reduced stimulation and passivity. The statement by Schreber is striking: "I wanted nothing whatever to do with any kind of miracle. They all filled me with disgust, particularly as I had made absolute passivity my duty" (page 145). These accounts are relevant in view of the growing body of literature on isolation and sensory deprivation.

TABLE V

Content and Circumstances of Hallucinations

Reference	Circumstance	Hallucination
Hillyer (24, p. 88)	Coming to consciousness after a long sleep, tied down to a bed in solitary confinement.	People that I was fond of passed me in the hall, they moved in swift procession on and on.
Graves (20, p. 182)	I was in a half-slumber.	An actual male person was in the sleeping room and had entered through the door.
(20, p. 190)	In strong cell.	A nurse in uniform sat in her watch chair in the outside hall, but slumped down while the ray beam shot over her. Leaning against the bars I watched intently while Dr. Percival and two or more internes solemnly draped in hoods of Ku Klux Klan style paraded up to the light source in turn, bowing and returning, and going through some peculiar stunts.
(20, p. 230)	I lay on the ground in a half-stupor, conscious of a blank mind.	I saw a patient named Jacobs who had talked with me on early hospital entrance soon to be discharged.
(20, p. 386)	During or after hot packs in hydrotherapy.	A clear visual hallucination of butterflies colouring some dead leaves.
Shreber (44, p. 107)	In bright daylight, I saw from my window . . .	A magnificent portico arise, as if the whole building were going to be transformed into a fairy palace.
(44, p. 145)	In broad daylight while I was sitting immobile on a chair.	I distinctly saw the polished brown surface of a grand piano in the making . . . I wanted nothing whatever to do with any kind of miracle. They all filled me with disgust, particularly as I had made absolute passivity my duty.
Jefferson (26, p. 236)	Tied in a strait-jacket in solitary confinement.	A disappearing radiator . . . a great bat flitting in and out behind a radiator . . . an imp jumping up and down.
J. Simpson (46, p. 69)	Alone in a room and half-starved.	Someone was laughing beside me, laughing and laughing.
Anonymous (11, p. 19)	Alone in the cold and darkness.	I thought I saw a chink in the wall through which light was streaming. I looked through it and there was a paved court with stables all around and troop horses tied to rings in the wall.
Custance (16, p. 45)	That night I had a vision. It was the only pure hallucination I had ever experienced. I woke up at about five o'clock to find a strange, rather unearthly light in the room.	I saw the great male and female organs of love hung there in mid-air . . . pulsing rhythmically in a circular clock-wise motion.

TABLE V—*continued*

Reference	Circumstance	Hallucination
Hennell (23, p. 55)	Alone in a cell.	The door opened and two of my friends entered; and they seemed to have diminished to half the size of men . . . they set to work to paint the body as it lay, in tiger stripes of black and yellow . . . the mummy then had a prodigious sexual orgasm.
(23, p. 72)	During the night while alone in a mental hospital room.	There entered my room and passed before me some sinister figures . . . during this night twice or thrice I was awakened by momentary brilliant flashes and at each occasion people stood nearby.
(23, p. 93)	Rising one night, I looked through a glass slit.	With his back to me stood a very broad-shouldered, short old man . . . He had been my earliest master, but had been dead for twelve years.

The narratives bear eloquent testimony to the struggle of the sick person to ignore his sense-data. The patient discovers that the reality presented to him by his eyes and ears differs from the reality that others perceive. He could resolve his dilemma in three ways: he could attempt to ignore his personal (asocial) reality (e.g. by following the frequent advice of "Don't listen to the voices"); he could acknowledge the reality of the visions, but say nothing about them to other people (e.g. adopting the position that there were two realities, social and personal. Here he would be following the advice frequently offered by one patient to another, "Don't say anything about them to the doctors or they'll think you are crazy"); finally, the person could choose to believe his sense data and act accordingly. This leaves him open to the response encountered by Moore, "We are going to keep you here and shock you until you forget those ideas."

There is, of course, nothing unusual in having to learn to ignore sense data. In flying at supersonic speeds the usual cues of balance become unreliable. If he is to survive, the pilot ignores his proprioceptive cues and relies exclusively on his instrument panel. Even experienced pilots will at times forget this dictum and feel that they are losing altitude when their instruments report that they are flying level. At very great speeds the person may be flying sideways or upside-down without being aware of it. Pilots practising in Link trainers for blind flying are taught to accept their instruments and disregard sensory cues.

The mentally ill person lacks an instrument panel with which to gauge reality. There are several choices open to him. He may attempt to use other people's judgments to secure some kind of consensus. We found numerous instances where patients asked attendants whether they had seen certain objects or heard certain sounds. The patients also tried to devise objective tests of their percepts. Boisen mentioned how he saw a cross on the moon and attempted to verify this by asking the attendant about it. He checked further by looking at the cross from various positions. He soon realized that the cross was due to a hole in his window screen and traced his recovery to this episode. Graves mentioned how he felt that there were rays surrounding him and he attempted to learn more about these rays by moving to various parts of the room and noting their intensity. Judge Schreber described his feelings of being turned into a woman and continually suggested that medical authorities examine his body to see if this were true. No one accepted the challenge and to the end Schreber believed in this change of sex. The same held true for his beliefs in his loss of weight. "I believe I could have been more rapidly cured of certain hypochondriacal ideas with which I was preoccupied at the time, particularly concern over loss of weight, if I had been allowed to operate the scales which served to weigh patients a few times myself; the scales used in the University Clinic at the time were of a peculiar construction unfamiliar to me" (page 62). In book after book these authors made constant and even heroic efforts to gauge reality, to learn whether their senses were relaying false data. The struggle can be described as one of "senses versus consensus". The patient himself often measures improvement by the extent to which he is able to ignore his senses and believe the words of others. Thelmar (53) expresses this particular dilemma poignantly:

> The doctor, Mrs. W., and the nurse all endeavoured to reassure me. They declared everything was all right. I thought—"Now, what am I to believe—these people's assurances or my own senses? They say that letter is not written in three different handwritings, and that I am not talking in all sorts of different voices . . . well, I can see for myself those different writings, and hear myself unmistakably talking in those other people's voices. If it were only these women telling me it was all right, I should know at once what to think: they always say everything is 'all right' however wrong it may be. I cannot believe a word they say. But now this doctor—he has never lied to me. I can always believe what he says. He, also, declares it to be 'all right'. Now, what can it mean? Am I to believe what he says, contrary to the evidence of all my own senses? That would be simply irrational." (page 234).

For the sociologist these accounts contain a wealth of material on the mores of the hospital and the effects of a total social system upon its members. As one example of this, we will compare briefly the hospital as seen by patients with the prison as seen by convicts. We have read many books by former prisoners and hope to extend this sample. Mental hospitals have no mutinies, no special language, very few profitable small businesses, no large-scale escapes (the maximum seems to be two persons), no organized opposition to the staff, and a very ineffective grapevine (except perhaps on admission wards). Escape attempts in mental hospitals are extraordinarily crude; very little resourcefulness is shown in planning or implementation. Prisoners are more active sexually than patients, and homosexuality is more blatant in prison. Prison newspapers are usually well-written and compare favourably with most community papers. Mental hospital papers look as if they were written in kindergarten and contain little interesting news. Prisons take extreme measures to maintain silence and cut down communication. In spite of this, an elaborate communication network flourishes based upon smuggled notes, a grapevine in which guards participate, whispered messages at mealtime, and planned rendezvous at church or sick call. For example, we have seen several instances in which prisoners sign up for religious services or sick list simply to meet other prisoners. This is an accepted way of meeting someone in prison. Hospitals, on the other hand, are extremely concerned with increasing interaction and conversation between patients, and between patients and staff. Patients are encouraged to speak to others at occupational therapy, meals, or in the dayroom. In spite of almost heroic efforts on the hospital's part, these campaigns seem to have met with little success. One has only to walk through most wards and activity rooms to see how little interaction actually occurs. Probably the most striking difference concerns the special language or argot. No one reading a prison book can help noticing the special idiom employed. Some prison books contain a glossary for this reason. On his first day in prison, Nathan Leopold (7) was handed a note by another prisoner containing several key words and translations. British prison books seem full of expressions that an American reader cannot understand; however, this difficulty is not experienced with mental hospital books. The language is similar in American, British, or Canadian mental hospitals and is easily understood by the lay reader. Unlike prisons, children's camps, and army barracks, there is no special language among mental patients. The only possible exceptions are non-psychotic admission ward patients such as alcoholics and psychopaths who frequently use slang expressions of the outside world.

Prisoners are also insatiably hungry for news of the outside world. Norman (9) mentions how he and his fellow convicts went to great lengths to construct crystal radio sets, a practice forbidden by prison regulations. This can be contrasted with the struggle nurses have to get mental patients to listen to the radio and TV provided gratis by the hospital.

DISCUSSION

We have shown two ways in which these autobiographies can be used in clinical research, but this by no means exhausts the possible uses of these books. Some of the more promising avenues to be explored are:

1. Study of autobiographies from non-English speaking countries.
2. Comparison of fictional accounts with autobiographies.
3. Comparison of hospital accounts with those from prisons and tuberculosis sanatoria.
4. Comparison of patient autobiographies with accounts by people who have taken hallucinogenic drugs.
5. Study of autobiographical articles by mental patients.

An interesting feature of previous use of these books in psychiatric writing is that the authors have been more renowned as objects than as subjects. Several of them have developed coherent and potentially useful theories of psychopathology but these have received little attention. Custance's ideas on the relationship between the unconscious, creativity, and mental illness have been largely ignored, as have Boisen's theories on the relationship between religious inspiration and mental illness. While their experiences and feelings have been used to illustrate theories already held, their interpretations of these experiences have been largely ignored. This seems unfortunate, because it is precisely as subjects that these authors can be of greatest assistance. In no other field can one's subject matter assist so actively in the search for understanding.

These authors are uncommonly well-read people and are generally acquainted with psychiatric literature, not a few quoting liberally from Freud, James, and Jung. An interesting omission in their references is the work of other ex-patients. None of the authors makes a detailed comparison between his own experience and symptoms and those of other authors. This is anomalous, since the avowed goal of many of these writers was to convey their experiences to other people. It would, therefore, seem logical that they would take notice of what other patients have to say; however, the reader receives the impression that each author considers his experiences unique and beyond the realm of comparison. This is a similar attitude to many of those who have taken mescaline or LSD. They do not see how one experience can validly be compared with another. Although there are many individual accounts of mescaline and LSD in print, there are very few cross-references and no compendium as far as we know. A colleague pointed out the similarity between this situation and that of former inmates of concentration camps. To a man they doubt that any book written has fully described the experience of living in a concentration camp. Perhaps no books can ever capture the intensity of living in Dachau or even the thrill of mountain climbing. The same point may apply to our authors, who give the impression that no one else's experience would be of much value in describing what they saw and felt. This underscores another advantage of using these autobiographies in that we are dealing with relatively uncontaminated data. The curious fact that the authors paid little heed to one another's writings increases the research value of the series.

This should tell us something about the nature of schizophrenic communication and the efficacy of group psychotherapy. If we gathered these authors together in a psychotherapy group, one wonders how much benefit they would derive from it. Their experiences and feelings fall into the category of esoteric communication. Interestingly enough, the authors do not stress the difficulties their readers may have in comprehending the nature of their experiences. The narratives are rendered as factual accounts—this is what I saw and heard, and this is how I acted. The reader soon finds that if he accepts the patient's premises, which are his experiences and perceptions, his actions follow logically. In only a handful of cases are we faced with illogical acts or behaviours that are not understood by the author. When Jane Hillyer withdrew from the other patients and nurses, she was well aware of doing this, and why she was doing it. When Judge Schreber adorned himself with female ornaments, he felt this was quite proper since he had been turned into a woman.

These are not accounts of illogical and senseless behaviour, nor of random or frivolous acts. The patients lack neither goals nor reason. In case after case what has gone awry is perception. Given incorrect information from eyes and ears and all senses, the clearest sensorium cannot help but come to conclusions that appear strange to other people. When Moore saw his former teacher, Mr. Armstrong, who other people claimed had died, it is not surprising that Moore not only questioned the reports of Mr. Armstrong's death but also believed that his appearance indicated the importance of Mr. Armstrong's philosophy. To see someone who is dead not only indicates that the man is alive but also suggests that the man is divine. The only way this could be prevented is for the person to know that his senses are wrong.

There may be some objection that in doing this study we were using only "biased observers". This is, of course, true, but any observation, whether it be of a polar expedition or diplomatic intrigue, will be affected by the personality and motivation of the observer. Many of these ex-patients are in a unique position to describe a world that is unknown to most of us. Only a handful of psychiatrists and social scientists have entered a mental hospital as patients intent upon observing the world from the patient's standpoint. When this was attempted by a young anthropologist, his mentor complained that he identified himself so closely with the patients that his objectivity suffered (3). If the patient's view of the world is so different from that of the psychiatrist that it is able to win over a professional anthropologist, surely it deserves study as seen by those who know it most intimately. Some of these ex-patients are extraordinarily sensitive and gifted people. At least seven were professional writers, well qualified to describe a living social system such as a mental hospital. Furthermore, our goal is to learn how patients see and feel about their world, i.e. a subjective view. Some of these patients, as would be expected among any group of people, have axes to grind. Yet the axes are manifestly of different sizes and shapes. Several authors are intent upon exposing the brutality of attendants, while others offer extravagant praise to these selfless and dedicated men who make service to the mentally ill their careers. Several authors want to illustrate schizophrenic logic and perception. Others want to prove to the world that they were never mentally ill. A few, including two lawyers, discuss laws relating to mental illness and suggest various changes.

In essence, the author's attitudes toward mental hospital and psychiatry range along the entire spectrum from praise to hostility. Contrary to some opinions, the majority of books were *not* published by paranoids intent on exposing the system. Fully as many authors were interested in describing their individual psyches. In several of the books we could not find any description of life on a hospital ward.

We do not claim that these accounts are factual or that the authors are fully objective. Such conditions would be ideal in any case, and do not have to be assumed to use the autobiographies as data. No one expects eyewitness accounts of any event to be fully factual or objective. The most the researcher can do is obtain stories from a wide range of observers and collate them. If trends consistently emerge, the researcher may place a high degree of confidence in their physical or psychological reality. To understand the appeal of a charismatic leader, interviews with adherents and acolytes would be indispensable. Their avowed lack of objectivity and manifest bias would in no way decrease the value of their accounts for understanding the appeal of the leader to his followers.

These autobiographies can provide a solid foundation for constructing the *Umwelt* of the mental patient. There are so many recurring themes of interest to psychiatrists that we cannot even summarize them here. For example, Christmas seems a particularly hellish time for mental patients and hospital attempts at creating a holiday atmosphere on the wards only compound the misery. The patients and psychiatrists were using many words in quite different ways—"treatment" usually meant one thing to the patient and another to his psychiatrist. Schizophrenic patients were strongly affected by ambiguous designs and patterns, and several suggested that plain furnishings and drapery would have been more suitable for their rooms. Countless other suggestions could be listed. Some are good, some are impractical, but all stem from first-hand experience on a mental hospital ward. We can only recommend that the interested reader obtain several of the books for himself and learn from some very gifted teachers how the world appears to a mental patient.

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THE SENTENCE COMPLETION TEST: AN EXPERIMENT AND EVALUATION

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THE Sentence Completion Test is now a well-established technique. It is more than sixty years since Ebbinghaus (2) published the first completion test, which he used to assess mental abilities of schoolchildren in Breslau. But it was not until 1928 that the completion method was used for "personality" assessment, when a fifty-item test was used by Payne (11) as part of a guidance programme.

The method caught on slowly, and most of the experimentation was done in America. Levy (6) listed a hundred and thirty-five studies between 1946 and 1951, and in 1953 Bonnet (1) published an excellent review of the literature up to that time.

Although a few standard versions of the test have appeared, e.g. those of Rohde (13), Rotter (14), Holsopple and Miale (5), and Sacks (16) most experimenters have used versions of their own. One of the great advantages of the test is its flexibility: tests can be made up to suit the purpose of the experimenter.

It is not my intention to review the literature since 1953, but as the test has not been greatly used in this country, it may be worth while to mention some of the modifications introduced and some of the experiments carried out, including a recent one by the writer.

One modification, in the writer's opinion an unsatisfactory one, was to offer the subject a choice of completions—the "Forced choice" technique —which strikes at the root of the completion method. The essential feature of this method is the eliciting of "free" associations.

In the design of sentence-openings three main approaches have been used, either separately or in combination—the first person approach—"I am most at ease when . . . ", the third person approach—"John felt at ease when . . . ", and the impersonal approach—"People feel most at ease when . . . ". There have been differences of opinion about these.

Rohde (12) thought that the first person method put the subject on his guard and limited his freedom of expression, while the third person method relaxed his control and allowed him to project his needs, wishes, likes, dislikes and fears, etc., more readily-material which he would be unable or unwilling to bring out in the direct approach.

Stein (17) agreed with this, and his own third person approach yielded higher indices of maladjustment than the first person approach.

Sacks (15) on the other hand found that the first person items produced results more closely related to the criterion (psychiatric ratings); and 67 per cent. of his subjects chose the direct form as being a truer representation of their state of mind. In the third person items some subjects related their responses to actual people known to them. Because of this Sacks preferred the impersonal approach (above).

Getzells and Walsh (3) gave paired completion tests, i.e. "direct" (first person) and "projective" (third person) to their subjects. The former was said to provide a measure of overt attitudes and the latter of covert attitudes. A further metric was the Index of Differentiation, a measure of the discrepancy between the two: in a sense a measure of degree of repression.

For clinical use the writer favours the first person "stems". In disturbed subjects the emotionally charged material is near the surface waiting to be released. This method is very useful for subjects who are too shy to speak in the interview, or forget most of the things they wanted to say. In these cases the protocols may be made the basis of further interviews.

Scoring: There has been some controversy over the scoring of the sentence completion test. Holsopple and Miale (5) say "The procedure in dealing with sentence completions is a procedure of interpretation and is not a procedure of scoring . . . " the objectivity of many psychological instruments "has long been clearly, if quietly, recognized as illusory".

Rohde (13) says one cannot score a sentence completion record on the basis of instructions in a manual. Her own method based on Murray's schema (8, 9) of needs, "press" etc., is a very complicated one, which would require a good deal of training. Sacks (16) used a three-point scale for degrees of maladjustment—2 points for "Severely disturbed", 1 point for "Mildly disturbed", and nil score for "Not significantly disturbed".

Rotter (14) uses a seven-point scale covering degrees of adjustment and maladjustment. He gives criterion sentences to guide the scorer and there is a correction for omissions. Although such a scale gives a wide score-distribution it is less easy to score than a five- or three-point scale, and gives lower inter-scorer reliability.

Experiments, including the one to be described, show that semi-objective scoring of sentence completions is possible and useful for comparing both groups and individuals.

The score is only a part, perhaps the least important part, of the information accruing from the test; but the more important question of interpretation will be considered later.

Reliability: The "Split-half" or "Odd-even" methods of testing internal consistency are not relevant because of the great variety of themes covered. If, however, items are collected into categories such methods may be applied.

The test-retest method is also unsatisfactory. Rotter (14) found a retest correlation of +·81 after one week's interval (80 subjects). The correlation decreases with time. Osterweil and Fiske (10) found that after three weeks 80 per cent. of the responses were changed in some degree.

Validation: Various criteria have been used to validate sentence completions, from observer ratings to interview data. As with many other psychological methods correlations have not been impressive, and the question arises, which method is validating which?

Sacks (16) on a sixty-item first person test, obtained correlations ranging from +·45 to +·57 between psychiatric ratings and degrees of disturbance revealed by the test, as established by three psychologists.

Rohde (13) correlated each of several traits from the sentence completions with combined ratings, etc., from teachers, school reports, parents, interview, etc., and found mean correlations of +·78 for boys and +·82 for girls.

Rotter (14) obtained correlations of +·50 for girls and +·62 for boys between sentence completion data and instructors' ratings.

In clinical practice it may be better not to trouble too much about questionable methods of validation, but to incorporate the completion data in the total picture, i.e. along with clinical data from other sources.

THE PRESENT EXPERIMENT

For some time the writer had been collecting records from both normal and psychiatric subjects on a sixty-item test used for routine clinical appraisal, and from psychiatric patients only on a second sixty-item test designed to measure certain attitudes. I shall not be concerned here with these, except to say that they appeared to be rather too long.

Experience with these tests did, however, help to suggest a forty-item test which was given to three groups of patients, as follows:

Group A: Twenty patients attending the medical out-patients' department of a large general hospital. Seven had digestive disturbances, five respiratory, and there were cases of arthritis, diabetes mellitus, menopause, sterility, essential hypertension, etc. One case had been treated by electroconvulsive therapy for depression in the past.

Group B: Twenty neurotic and psychopathic patients attending the day hospital unit of an early treatment centre. They covered the usual range of ailments found in a psychiatric clinic—with anxiety states, phobic states, depression, hysteria, psychopathy, etc.

Group C: Twenty in-patients at the same centre. These were basically similar to Group B patients but were considered, in general, to be rather more disabled.

Each of the three groups was equally divided as to sex.

The general hospital group was older than the other two, with an average age of 48 as against 36 and 34 for Groups B and C. Group A were taken at random from the waiting hall, while Groups B and C were successive admissions. The samples are small, but the experiment was in the nature of a pilot study to see if the test data could differentiate between groups which appeared, prima facie, to differ in degrees of psychological adjustment.

There seem to have been few comparative studies with the test. A recent study by Luft, Wisham and Moody (7) of sixty-two miscellaneous male patients aged 19 to 65, showed psychiatric patients to be the most pessimistic on the test, followed by the gastro-intestinal and the cardiovascular cases, with surgical cases at the more optimistic end of the scale.

In another comparative study Goodwin (4) found that peptic ulcer cases showed more hostility than asthmatics.

Returning to the experiment: The responses from the three groups were scored on a three-point scale from plus-one for optimistic or "positive" responses, through zero for neutral responses, to minus-one for responses deemed to be pessimistic, etc. Samples of the three types of response are given later.

Of the forty items 11 were expected to produce mainly plus answers, 12 mainly negative answers, and 15 mainly neutral. The latter permit more freedom of response than the other two categories with the positive and negative ones about equal, as Table I shows.

The expected or theoretical mean score would be —3. For the whole group the obtained mean score was —2·4 points. Mean scores for the three groups were: Group A +2·2 points, Group B —2·4 points, Group C —5·0 points. These scores were in the expected direction.

TABLE I

Expected and Obtained Scores

Expected	No.	Obtained Percentage		
		+	0	—
Plus items	11	81·6	9·9	8·5
Zero items	15	41·4	21·4	37·2
Minus items	14	2·8	11·6	85·6

One cannot compare such small scores statistically, especially when signs are opposite, but a χ^2 test on the *total* scores shows the difference between the three groups to be significant at the 1 per cent. level of confidence. The best discrimination accrues from a comparison of negative ("maladjustment") scores, as will be seen from Table II.

TABLE II

Total Scores for the Three Groups

Group	Scores				
	+	0	—	Omissions	Total
A	302	132	259	107	800
B	277	109	326	88	800
C	294	86	394	26	800
	873	327	979	221	2,400

SEX DIFFERENCE

As Table III shows, there was no sex difference on overall scores but on neutral scores the sex difference was statistically significant at the 1 per cent. level of confidence.

TABLE III

Scores for Male and Female Patients

	Scores				
	+	0	—	Omissions	Total
Female patients	430	139	493	138	1,200
Male patients	443	188	486	83	1,200

Age: The correlation between age and scores for the total group was +·325. In the psychiatric groups there was a definite tendency towards higher scores or better adjustment with age (day patients "r"=+·572, in-patients "r"=+·658), but in the general hospital group there was no such tendency ("r"=+·014).

INTELLIGENCE

The correlation between intelligence—as measured by a selective vocabulary test—and degrees of adjustment showed little relationship ("r"=+·049).

OMISSIONS

The sentence completions form one side of the picture: on the other side are the omissions. The overall omission rate was 9 per cent., which compares favourably with 25 per cent. on a sixty-item test. And there was no increase in omissions through the test, as in the longer one.

Significantly higher omissions ($p = \cdot 01$) were found in the records of female patients—all groups—and in those of the general hospital patients.

The correlation between intelligence and omissions is $-\cdot 253$, i.e. slightly higher omissions in patients of lower intelligence.

The negatively-loaded items, as one might expect, produced more omissions than the neutral or positive-loaded items (13 per cent., 8 per cent. and 5 per cent. respectively).

Neither age nor scores on the completion test showed much relationship with omissions ("r"$=+\cdot 136$ and $+\cdot 093$ respectively).

ITEM ANALYSIS

The responses to each item were recorded on cards and examined for group and sex differences and for evidence of the usefulness or otherwise of the items. In view of the fact that item analysis reduces the sample, only broad trends can be noted.

The forty items with sample responses are as follows: in some instances answers were almost wholly negative or almost wholly positive, in others all three types were encountered. In the latter case some examples of plus, negative and minus answers are given.

1. What puzzles me is:
    Why the evolutionary process has not reduced illness.
    Why the world is in such a hurry.
    Why I can't keep going.

2. My best friend would say I:
    Have a happy nature.
    Am a silly woman.
    Wonder how . . . is?

3. My happiest moments:
    Are with my home and family.
    When collecting my winnings.
    When I am making things.

4. What annoys me most is:
    Bragging and selfishness.
    People who are the centre of attraction.
    Myself.

5. I dislike people who:
    Say one thing and mean another.
    Run other people down.
    Push others around.

6. If I had the chance I would:
    Start all over again.
    Become a professional singer.
    Make my husband happy.

7. My childhood was:
    Carefree
    Lonely.
    Happy but strict.

8. I am most at ease when:
    I am at home with my friends.
    Listening to classical music.
    In the company of men.

9. Most men:
    Are good and kind.
    Want too much waiting on.
    Bah!

10. The worst thing I ever did:
    Was to run over a child.
    Was to steal from a poorer man as a P.O.W.
    Take an overdose.

11. In company I:
    Feel relaxed.
    Feel lost.
    Am on edge.

12. To me sex is:
    A beautiful and wonderful thing.
    All right in its place.
    Over-rated.

13. I suffer:
    From head pains and indigestion.
    Fools gladly.
    But others suffer more.

14. I have always wanted to:
    Be best at everything.
    Go abroad.
    Have a home and children.

15. I am embarrassed when:
    People stare at me.
    I see people half naked.
    In the presence of my superiors.

16. The people I like best:
    Are those who like children.
    Are trustworthy, honest, etc.

17. Married life is:
    Wonderful.
    What you make it.
    All mixed up.

18. I envy those who:
    Are fearless, unruffled, have no worries, etc.

19. I can't understand what makes me:
    Feel inferior.
    So frightened.
    Aggressive, depressed, etc.

20. To me the future looks:
    Hopeful, doubtful, black, etc.

21. I feel I might have failed:
    - As a wife and mother.
    - To live up to my ideals.
    - But for my wife.
22. I believe I am best at:
    - Housework, understanding people, worrying, nothing, etc.
23. I secretly:
    - Wish I were romantic.
    - Long to erase the past.
    - Wish to get married.
24. My mother:
    - Is kind and generous.
    - Is strict and possessive.
    - Has too much to say for herself.
25. My life at home is:
    - Happy, etc. (in 70 per cent. of cases).
26. I have a fear of:
    - Passing out in the street.
    - Getting old.
    - Going insane.
27. When I am alone I:
    - Like to plan for the future.
    - Think of all the dreadful things I've done.
    - Sing opera.
28. Most women:
    - Are kindness itself.
    - Consider me incapable.
    - Think they are "it".
29. At school I:
    - Did well at games.
    - Had moments of glory.
    - Was made to feel small.
30. The best thing I ever did:
    - Was to save a child from drowning.
    - Was to finish a forced march as a P.O.W.
    - Pass my driving test.
31. I have a habit of:
    - Analysing everything.
    - Picking my skin.
    - Putting people on a pedestal.
32. My greatest weakness:
    - Is getting up in the morning.
    - Is self pity.
    - Is giving things away.
33. I am determined to:
    - Get better (mainly).
    - Get on in life.
    - Do all I can for my child.

34. My father:
    Is very dear to me.
    Is not interested in me.
    Is a drunken brute.
35. There are times when:
    I could scream.
    I feel like giving life up.
    The future looks bright.
36. My worst enemy might say:
    He is not bad.
    I have only myself to blame.
    I am putting it on.
37. My greatest regret is:
    I can't have children.
    I didn't learn a trade.
    I married the wrong man.
38. I get panicky if:
    I am on my own.
    I have to entertain.
    If any of my family are ill.
39. What I want most in life:
    Is to get better.
    Is to live in a decent district.
    Is to see my son grow up.
40. I look forward to:
    Getting better.
    Going back to work.
    My holidays.

Discussion of Results

It has been mentioned that the *group differences* appeared most clearly in the negative items. The general hospital group managed to resist the negative "suggestion" quite often, especially in such items as "The worst thing I ever did", "I suffer", "I envy", "I feel I might have failed", etc. In other words they had more optimistic replies than the other two groups. On the other hand the psychiatric groups, especially the in-patients, revealed their pessimism even in items like "My best friend would say I" or "I have always wanted . . . ", etc.

The psychiatric groups were, in general, more self-centred, and self-depreciatory. Self-reference was expressed obliquely as well as directly, by projection or generalization, e.g. "What puzzles me is . . . why some people have to suffer".

There was also more self-pity expressed by the psychiatric patient including items such as "What puzzles me is . . . Why God should leave me like this". Their complaints were almost entirely psychological, while general hospital patients complained more of physical ailments.

The general hospital group omitted more items than either of the other two groups. This agrees with the findings by Wilson (18). Just why this is so is open to question. One might speculate that there is more pressure to respond in the psychiatric patients.

Although there was no overall *sex-difference* in degree of adjustment, item analysis revealed certain trends. Female patients had significantly less neutral responses. They also appeared to be more altruistic, especially in relation to their families and friends, more preoccupied with their homes and letting their families down, more modest, rather more concerned over sexual misconduct (not mentioned by men), more derogatory about their own sex, more prone to blame themselves. No compulsive trends were mentioned by men, but were brought out by six of the female psychiatric patients, especially in Item 31 "I have a habit of . . . ".

The above results show that the completions can discriminate both quantitatively between groups of patients, and between the sexes.

Apart from this the experiment yielded some useful information on the following points: 1. Length of test; 2. Lay-out; 3. Item selection; 4. Interpretation of protocols.

1. *Length of Test*

It is impossible to say what the optimal length of a test may be, because it is affected by the number and type of items, and the subject—his age, sex, intelligence, mood, need to communicate, the time of day and so on. Also, subjects in some countries are more test-conditioned than others. Some subjects complained about the length of the 40-item test. If the omission rate increases steadily through the test this may be one criterion of fatigue, boredom, irritation, etc.

A test which can be accommodated on one side of, say, a foolscap sheet, i.e. with 30 items, might be more acceptable. Some of the patients showed signs of displeasure when they found that there were more items on the back of the sheet.

2. *Lay-Out*

The early items of a completion test should be comparatively innocuous, cushioning possible shocks and leading the subject from superficial to deeper levels of functioning. In normal records defensive tactics in the early stages are fairly common, e.g., flippancy, superiority, evasion, etc., but in most instances the subject slips into a more serious mood, often touching on personal problems without, perhaps, realizing it. It is interesting that in the present experiment there was only one flippant response out of more than two thousand, i.e. "What puzzles me is . . . how many beans make five".

Although, ideally, every item should count, i.e. produce a good crop of useful information, it may be desirable to include a limited number of items as buffers, cross-checks, etc.

The *instructions* should be brief. It has been found that projection varies inversely with the exactness of the instructions. It has also been found that emphasis on speed does not produce better results. Early versions urged subjects to work quickly so that they would be less inclined to censor their responses. Rotter (14) found that stress on immediate response tends to produce short answers.

Space may be provided at the end of the test for comments which the subject may wish to make. Some of these are very revealing.

Anonymity is also desirable, though many subjects, given the choice to record name or initials, give their full names without compunction. It helps to reassure the patient if the word "Confidential" appears prominently at the top of the test blank.

3. *Item Selection*

It transpired, on examination, that nearly half of the forty items had some unsatisfactory features.

Thirteen of the items, twelve of them neutral, were dichotomous. Although they yielded a wide range of scores, they produced a narrow range of ideas, perhaps as narrow as a choice technique would have revealed. But there were instances where the wording of the responses was informative, e.g. "My mother . . . is the best friend I have", or ". . . drinks too much".

Six of the items, five of them negative, proved to be monothematic and, therefore, not very informative either, e.g. "I can't understand what makes me . . . like this", etc., or "I am determined to . . . get better", etc.

Twenty-one mixed items were polythematic, e.g. "What puzzles me is . . . ", "I envy those who . . . ". Although such items may yield a wide range of answers, they may not be very useful for group comparisons. It is less easy, too, to pick out unique responses when there are almost as many categories as individuals. For this a larger sample would be necessary.

It looks, therefore, as if dichotomous and monothematic items are better for group purposes, while polythematic items are more suitable for qualitative interpretation.

Some items were quite obviously redundant, eliciting information almost identical with that from other items, e.g. "If I had the chance I would . . . ", "I have always wanted to . . . ", or "I have a fear of . . . ", and "I tend to get panicky if . . . ". Redundancy also occurred through opposition of items, e.g. "I am most at ease when . . . ", and "I am embarrassed when . . . ". There were other similarities, but not all of them could have been predicted from the wording of the "stems".

A few items were ambiguous as to scoring, e.g. "I dislike people who . . . ", or "What annoys me . . . ". Since most of the traits mentioned were undesirable, it seemed more logical to award a plus score rather than a minus to such items.

Some of the items, irrespective of their position in the test had a high omission rate, e.g. "I secretly . . . (33 per cent.)," "My worst enemy might say . . . " (25 per cent.), "The worst thing I ever did . . . " (22 per cent.). In items such as these one has to decide whether or not the information obtained outweighs the reduction in responses.

Item Criteria: Some criteria of "good" or informative items can now be formulated:

(*a*) Phrases should be short and the wording simple.

(*b*) Items should not be "overstructured" so that they leave the subject little freedom of response, e.g. "My worst enemy would call me a . . . ". Such items may arouse irritation or evasion. Nor should they be understructured so that the subject may be embarrassed by too much freedom, e.g. "I . . . ", "When I . . . ", etc.

(*c*) There should be no overlap between items unless it is designed for special reasons.

(*d*) They should not encourage clichés, e.g. "money . . . is the root of all evil".

(*e*) They should not put the subject on the defensive so that he censors his response or omits the item.

(*f*) They should lend themselves to unambiguous scoring.

(*g*) They should differentiate between individuals and, if possible, between groups also.

(*h*) They should, in the writer's opinion, be framed in the first person for clinical use.

(*i*) There should be a mixture of positive, neutral, and negative items so as to allow the subject to display both his assets and his liabilities.

4. *Interpretation*

In the sentence completion test, as in any other projective technique, interpretation of the individual protocol is essential; the material can be very revealing.

During the last war the test was used in both American and British armed forces. The records were unscored but were scrutinized for pointers or trouble spots.

In a forced choice method one can rarely be sure of the significance of ticks or underlinings. There is no guarantee that they reflect what was in the subject's mind when he did the test. If he is bored, angry, confused or preoccupied he is likely to underline or tick at random. Written responses, even censored ones, are at any rate the subject's own, and tell us more about him. Most subjects when faced with an unfinished sentence have an urge to finish it—in Gestalt terms to effect a closure, though they may not always write their first thoughts.

Long experience with the test gives a background against which protocols become more meaningful and interpretations more valid. It enables one to sharpen one's inferences.

The test has an affinity with other projective methods such as the Rorschach Test and the free association method. One can, for instance, record common and original responses, and conduct an inquiry on the basis of the answers. Formal aspects can be dealt with, e.g., style, grammar, logic, spelling, etc.

Perhaps the most fundamental difference between the records of normal and abnormal subjects is in the degree of emotional detachment. Normal subjects tend to censor their answers more. But even here defences tend to be lowered as the test proceeds. The detachment allows them to be facetious, or critical, e.g. "My father . . . is a likeable rogue", "A husband . . . yes please", "What puzzles me is . . . what you expect to get out of this". This type of response may, of course, be a way of impressing the examiner, or of releasing tension, as well as a sign of relaxation and good spirits.

Anxiety shows itself in most records to some degree. It is less ego-involved in normals. A good example comes from a record of a normal subject temporarily away from home, who communicated a source of anxiety in three successive items: "I feel . . . anxious about my tomato seedlings", "At night . . . the temperature is about 50 degrees", "My worst . . . mistake was in sowing earlier than the instructions".

Sentence completions reveal not only areas of disturbance but also attitudes to certain situations, emotional modality and intensity.

Although, in interpreting the completions one is not concerned primarily with diagnosis, it is not too difficult to find signs pointing to the main diagnoses.

There are, for instance, the loose associations, denial of symptoms, irrelevance, negativism, etc., of the schizophrenic, the pessimism and paucity of response of the depressed person, the self-display or dramatization of the hysteric; anxiety, guilt, hypochondriasis, aggression, etc.

A well-designed completion test is a useful clinical instrument, and may be presented to the subject fairly soon after admission so that the doctor can, if he wishes, make use of the protocol in his interviews with the patient.

The test seems to be well received on the whole, more so than many questionnaires or inventories. The information received is more specific than that from, say, the Rorschach or the T.A.T. The writer can confidently recommend the use of a well-designed sentence completion test in conjunction with other projective tests such as those just mentioned.

Summary

The Sentence Completion Method of personality appraisal and some modifications of the original technique have been outlined.

An experiment with a 40-item test on three groups of patients has been presented, with some quantitative and qualitative comparisons. It has been suggested that the completion method can differentiate between patient-groups, but that the interpretation of the individual protocol is perhaps the most valuable part of the information obtained from the test.

Suggestions have been made regarding the optional length of the test, the lay-out, and selection of items.

Acknowledgments

I wish to thank Dr. J. J. O'Reilly, Medical Director, Uffculme Clinic, for permission to test psychiatric patients, and Dr. G. W. Hearn, Consultant, Dudley Road Hospital for allowing me to see "medical" patients under his care. Special thanks are due to Dr. D. A. Kent of Middlewood Hospital, Sheffield for advice in the preparation of the test and for help in scoring responses.

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COMPARATIVE HYPNOTIC EFFICACY OF "PHENAGLATE"

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INTRODUCTION

THE widespread use of barbiturates as hypnotics for insomnia has greatly increased the risk of accidental overdosage and the number of suicidal attempts. The size of the problem concerning barbiturates and suicidal attempts is difficult to estimate as only suicidal deaths are recorded by the Registrar General, and his statistics for 1956 (R.G., 1958) reveal that out of a total of 5,282 suicidal deaths, drugs (mainly barbiturates) were second only to domestic coal gas poisoning as the effective agent. Stengel (1958) calculated that six times the number of suicidal deaths gives an approximate estimate of the number of attempted suicides. Locket and Angus (1952) found that of the patients admitted to their Unit, barbiturates were the drug involved in 80 per cent. of the cases and that in 90 per cent. of the cases it had been prescribed for the treatment of insomnia. Locket (1958) also estimated that some 6,000 patients were admitted annually to hospitals in England and Wales for treatment of barbiturate poisoning.

Less toxic, but equally effective hypnotics, would be one method of decreasing the danger inherent in prescribing barbiturate hypnotics. An alternative approach is the simultaneous oral administration of a barbiturate combined with a barbiturate antagonistic.

The use of central analeptics in the treatment of barbiturate intoxication has been the subject of both clinical and experimental studies in man and animals. Nilsson (1951) and Locket (1952) prefer to rely on medical management, without using analeptics, in the treatment of severe barbiturate intoxication, whilst support for this approach is found in the demonstration of a depressant effect on the central nervous system of rabbits, following the initial stimulant effect of nikethamide, caffeine and leptazol (Maloney, 1935).

Contrary views are held by Koppanyi and Fazekas (1953) who found that the simultaneous oral administration of barbiturate and leptazol prevented death in dogs compared with controls receiving the same dose of barbiturates without leptazol. The same authors found in human subjects that with a ratio of leptazol to barbiturates 3:1 and 1·5:1 using a dosage of 200 mg. of barbiturates, sleep was not disturbed and that narcosis was delayed or prevented when the combination was compared with barbiturate given alone. Following the introduction of bemigride (β-β-ethyl-methyl-glutanimide), a much stronger analeptic, by Shaw *et al.* (1954) the drug was successfully used as a barbiturate antagonist in anaesthesia (Harris, 1955), in continuous narcosis in schizophrenia (Trautner *et al.*, 1957) and in barbiturate poisoning by Shulman *et al.* (1955). Following Shaw and Shulman's original work on bemigride, Trautner found that a combination of barbiturate and 12 per cent. bemigride lessened the depth and duration of sleep in human volunteers from 18 hours to 10 hours. Most of the work done on the combination of analeptics and barbiturates had, as its main clinical concern, the prevention of death in patients admitted with barbiturate overdosage.

As indicated above, the development of a hypnotic drug combination which allows effective application of the hypnotic element and at the same time supplies its own equally effective antidote should overdosage occur, seems a useful therapeutic advance in preventive medicine. The introduction of "Phenaglate" (quinalbarbitone sodium 50 mg., phenobarbitone 25 mg., bemigride 7·5 mg.) allowed the present authors the opportunity of determining the hypnotic efficacy of this drug compared with the same dose of barbiturate.

METHOD

Thirty-one psychiatric in-patients requiring a hypnotic from two associated, separately staffed hospitals, were the subjects of the trial. Administration of the drugs was by randomized order (Latin square) and a self-controlled double-blind technique was used. The drugs were each given 6 times during a 24-day period and the identical looking capsules were constituted as follows:

(A) "Phenaglate", 2 capsules.
(B) "Phenaglate", 1 capsule, placebo 1 capsule.
(C) Quinalbarbitone sod., 50 mg. phenobarbitone 25 mg. 2 capsules.
(D) Quinalbarbitone sod., 50 mg. with phenobarbitone 25 mg., 1 capsule, 1 placebo capsule.

Sleep recording was done by the night nurse who, on a prepared chart, assessed the patient at ½-hourly intervals as asleep or awake. A "broken" night was defined as a night on which a subject woke between periods of sleep and a "restless" night was that recorded as such by the nurse.

RESULTS

Drug	Mean Minutes to Fall Asleep/ Subject/ Night	Mean Minutes Awake/ Subject/ Night	No. of "Broken" Nights	No. of "Restless" Nights
Barbiturate 150 mg.	32	91	51	24
"Phenaglate" 150 mg. ..	40	99	62	30
Barbiturate 75 mg.	37	106	65	25
"Phenaglate" 75 mg.	34	104	72	41

As regards the mean time awake the difference between barbiturate 150 mg. and barbiturate 75 mg. is significant at the 5 per cent. level (using the correlated t test); that between "Phenaglate" 150 mg. and "Phenaglate" 75 mg. is not significant nor is the difference between barbiturate 150 mg. and "Phenaglate" 150 mg.

DISCUSSION

No data are given on the age or sex or in which hospitals the patients were treated, as a previous study on the comparative efficacy of hypnotic drugs failed to reveal any statistically significant differences between two groups compared for these factors (Lodge-Patch *et al.*, 1959). In the present study no period in which placebo alone was given appears. The reason for excluding such an apparent control is based on the findings of Hare (1955) who found that the comparative response to two hypnotics remains constant during a trial and that new hypnotics may therefore, be compared with a standard barbiturate preparation, obviating the necessity of a placebo. Hare also found that a high positive correlation was found between the night nurse's record of sleep and the patient's self-administered record in a double-blind trial, irrespective of whether a hypnotic or placebo was administered.

The results of the present trial show that "Phenaglate" at the higher level of dosage (2 capsules) is almost as efficacious as the equivalent dose of barbiturate, though there is a slight suggestion in the figures that the patients on "Phenaglate" slept less well.

The failure to find a significant difference between the two dosage levels of the "Phenaglate" prescribed is an anomalous feature which suggests that further confirmatory trials are worthwhile to clarify more precisely the comparative efficacy of "Phenaglate".

Having found that "Phenaglate", at a dosage of 2 capsules, is efficacious as a hypnotic, the question which remains and which this study has not attempted to answer is whether a patient taking an overdose of "Phenaglate" will escape a fatality which would result from an equivalent dose of barbiturate alone. The evidence from the literature presented above warrants the conclusion that the therapeutic principle represented by such a combination as "Phenaglate" has a future in its application to clinical practice.

In view of its epileptogenic effect on the EEG of patients and the reports of grand mal seizures in known epileptics (Gershon and Shaw, 1957) its use in this group of patients should be avoided.

SUMMARY

By use of a double-blind technique and randomized order, the comparative efficacy of "Phenaglate" with barbiturate has been tested at two levels of dosage. The failure to show any significant difference between the two, at the double level of dosage, suggests that "Phenaglate" is an equally effective hypnotic and in view of its containing a barbiturate antagonist, its value as a hypnotic is suggested for patients with insomnia who might be considered a suicidal risk.

ACKNOWLEDGMENTS

To Mr. W. Brookes and Mrs. K. Vejs, Pharmacists, Maudsley and Bethlem Royal Hospitals, also to A. and G. Nicholas Limited for supplying both the "Phenaglate" and the control capsules.

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DMAE (2-DIMETHYLAMINOETHANOL) IN THE TREATMENT OF CHRONIC FEMALE PATIENTS IN A MENTAL HOSPITAL

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WORK with the tertiary amine arecoline is reported to show that this parasympathomimetic agent can produce inhibition of conditioned avoidance responses in rats (Pfeiffer and Jenney, 1957a). When given to atropine-protected patients, the compound is said to give intervals of lucidity of an order broadly comparable to that produced by carbon dioxide or amylobarbitone (Fulcher *et al.*, 1957).

These results encouraged Pfeiffer *et al.* (1957b) to investigate other compounds which might be regarded as possible precursors of acetylcholine. 2-Dimethylaminoethanol (DMAE), already reported as substituting for choline in certain nutritional conditions, was shown to diminish convulsant thresholds and change EEG activity in experimental animals; these effects were not obtained from choline. DMAE given orally to man in doses of 20 mg. per day produced, in 7–10 days, central nervous system stimulation and lessened fatigue; in dosage above 20 mg. a day, muscle tone increase and insomnia were noted; with daily dosage of 250 mg. reduced to 50 mg., schizophrenic patients showed increased motor and verbal activity, and insomnia.

Lemere and Lasater (1958) described a preliminary trial of DMAE in depressed patients. Improvement within a few days in some cases of mild depression and nervous exhaustion, but not in severe depression, was reported on average daily dosage of 25 mg. They did not observe any false euphoria, drug dependency, or interference with sleep or appetite. Oettinger (1958) reported marked beneficial effects on the behaviour of children with epilepsy, and/or behaviour disorders, with several months' administration of the drug; the epilepsy itself was unaffected, or in some instances of grand mal made worse.

Two salts of DMAE are at present marketed in Great Britain: it was decided to exhibit the bitartrate to chronic psychotic patients.

From two female static wards twenty-six patients were chosen as suitable for testing the effects of DMAE. They had been in hospital for periods ranging from 3 years to 36 years (mean 22 years). Their ages ranged from 31 years to 83 years (mean 65 years). Some of these patients carried a diagnosis of depression and had had courses of E.C.T. from time to time. At the beginning of the first period these patients were all depressed in varying degrees. One patient had a diagnosis of epilepsy and psychopathy. The remainder had been diagnosed originally as schizophrenics. Most of these had had E.C.T. from time to time, and two had been leucotomized. All these patients not having the diagnosis of depression were characterized by prolonged and unremitting lack of volition, inactivity, emotional apathy and lack of interest in the ward or hospital affairs.

A standardized psychiatric interview was devised to ensure that as far as possible each interview would cover the same points of attention and interest. Each patient had an initial psychiatric assessment four weeks before receiving the drug. Thereafter she was re-examined, using the standardized interview, at the beginning of the first period and at monthly intervals for three further examinations.

The nurses' reports were standardized by using a modified version of the Fergus-Falls Behavioural Rating Scale. After a preliminary assessment this scale was filled in weekly for each patient.

Six patients with the diagnosis of depression and eight others were given DMAE. The remainder acted as controls.

It was felt that the difficulty in maintaining secrecy when using placebos possibly confuses issues as much as it elucidates them. For this reason placebos were not given to the control patients. They were interviewed by the psychiatrist and assessed by the nurses in the same way as those in the experimental group. The possible effects of increased attention in the trial group were thus counterbalanced at least to some extent. Moreover, the semi-structured nature of the psychiatric interview possibly helped also to guard against such an "interest arousal" effect.

For the first four weeks of the test period each of the patients in the experimental group was given 40 mg. of DMAE daily. For the remainder of the test period the dose was increased to 80 mg. daily.

Following a suggestion by Pfeiffer that DMAE therapy might be more effective when biochemical adjuvants were found to increase acetylcholine synthesis, the use of methionine as a possible methyl donor was next considered.

To test this possibility two grams methionine daily were given to six patients in the experimental group and four in the control group for a period of eight weeks, beginning at the end of the first month of the test.

RESULTS

Towards the end of the trial period one of the patients in the experimental group had a recurrence of depression necessitating E.C.T. From her history this recurrence could have been expected at this time. One of the patients in the experimental group was regarded by the nurses as being more alert and interested in herself towards the end of the test period. Apart from these changes which are statistically insignificant, no alteration was noted in the affect, attitude or behaviour of any of the remaining patients in either group.

SUMMARY

The substance 2-Dimethylamino-ethanol (DMAE), a possible precursor of acetylcholine, was given to a group of fourteen chronic female patients in a mental hospital in doses of 40 mg. daily to each patient for four weeks, and 80 mg. daily for a further twelve weeks.

Methionine 2 grams daily in addition to DMAE was given to six of those patients and to four patients in a control group for a period of eight weeks during the test period. With twelve patients acting as controls, each patient was assessed independently by a psychiatric interview and by nurses' reports.

CONCLUSION

DMAE (2-Dimethylamino-ethanol) as given in the circumstances of this test had no significant effect on chronic female patients in a mental hospital.

ACKNOWLEDGMENTS

I am indebted to Dr. A. C. Tait, Director of Clinical Research, for advice and help in the conduct of this trial; to Dr. J. Harper, Physician Superintendent, Crichton Royal, for permission to publish this paper; to the nursing staff for their interest and help; and to Messrs. Duncan, Flockhart & Co., whose generosity made the drug available for trial.

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A PILOT TRIAL OF ORPHENADRINE ("DISIPAL") IN PATIENTS TREATED WITH RESERPINE

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β-DIMETHYLAMINE ethyl 2-methylbenzhydryl ether hydrochloride (Orphenadrine, "Disipal") is a synthetic substance closely resembling in chemical structure the antihistamine dephenhydramine ("Benadryl"). It was developed in Holland (Harms, 1957) for use in parkinsonism and in this context reported upon favourably in this country by Gillhespy and Ratcliffe (1956). Claims have also been made that the drug is (*i*) effective in treating the pseudo-parkinsonism produced by reserpine, (*ii*) active in alleviating other (e.g. autonomic or vasomotor) side-effects of reserpine, (*iii*) has independent "psychic" activity, or (*iv*) enhances the tranquillizing effect of reserpine (Frieswinkel, 1957a, 1957b; Van Rhijn, 1957; Meulenbeld, 1957; Scheurle, 1957). The following trial is designed to assess some of these claims.

SELECTION OF PATIENTS AND METHOD

As reserpine is slow to achieve its maximum therapeutic effect (Elkes, 1957; Kovitz *et al.*, 1955; Arnold and Freeman, 1956; Koltanow, 1956) and initially irregular in activity, e.g. a "turbulence phase" may occur (Barsa and Kline, 1956; Naidoo, 1956), only patients were chosen who had been treated with this drug for at least four weeks. These were ten in number and all females. Nine of the ten had, in fact been treated with reserpine for several months before the start of the trial. Two patients were receiving 2 mg. reserpine t.d.s., six were receiving 1 mg. t.d.s., and the other two 0·5 mg. of reserpine thrice daily. These doses were maintained during the trial. Actuarial data and diagnosis of the patients are shown in Table I.

A "double blind" technique was employed and patients were in addition to their reserpine treated in random order with either Orphenadrine tab. 1 (50 mg.) t.d.s., or matched placebo tab. 1 t.d.s. for three weeks after which the treatment was switched to the alternative tablet for a further three weeks.

The patients were examined by the investigators at weekly intervals, each doctor seeing the same group throughout the trial. Results were assessed with the Fergus Falls Behaviour Rating Scale (Lucero and Meyer, 1951) a check list of toxic symptoms and a timed test of motor performance (drawing twelve parallel straight lines without the aid of a ruler). The behaviour rating scale was completed in part by the senior ward nursing staff and in part by the Occupational Therapists. The remaining observations were made by the investigators.

TABLE I

Clinical and Actuarial Data

No.	Patient	Age	Daily Dose of Reserpine (mg.)	Period on Reserpine Before Treatment in Weeks	Duration of Illness in Years	Diagnosis from Case Records
1	G.B.	45	6	88	17	Schizophrenia
2	M.G.	26	6	88	13	Schizophrenia
3	G.B.	40	3	52	35	Schizophrenia
4	J.P.	29	3	56	9	Schizophrenia
5	G.P.	74	3	76	6	Confusional psychosis
6	F.S.	75	3	36	9	Chronic depression
7	A.B.	37	3	24	16	Propf-schizophrenia
8	E.H.	38	3	44	4	Schizophrenia
9	S.B.	31	1·5	4	4	Schizophrenia
10	M.Q.	70	1·5	20	19	Hysterical psychopath

RESULTS

(a) *Behaviour Ratings*

No precise information was available and it appeared possible that orphenadrine could have a "carry over" effect persisting after the drug was discontinued. The ratings of the first two weeks in the placebo period (which in half the cases followed the drug period) were, therefore, ignored and all comparisons were made with the third week of the placebo period. In nine items of behaviour rated on a five-point scale, means and standard deviations for each week on orphenadrine plus reserpine were compared with the mean and standard deviation of the scores obtained in the third week on placebo plus reserpine (Table II). No significant differences were found between the group scores for the period on the drug and the placebo period (lowest value of p=0·1–0·2). Examining the significance of the *differences* between placebo and drug scores in the same patient, one set of differences was found to be significant (at the ·05 level) in 27 examined. This showed a deterioration in "speech" when on the drug, but this finding could clearly be due to chance and there is no reason to attach any special significance to it.

TABLE II

Behaviour Ratings (Means and S.D.)

	Orphenadrine			Placebo
	Week 1	Week 2	Week 3	Week 3
Work	2·5±0·81	2·9±0·56	2·0±0·77	2·3±1·10
Response to meals	2·9±1·22	2·8±1·66	3·1±1·34	2·9±1·45
Response to other patients	2·4±1·56	2·5±0·07	2·8±1·53	2·2±0·75
Response to nurses	2·3±0·78	2·3±0·78	2·2±0·98	2·2±0·66
Response to treatment	3·3±0·63	3·1±0·10	3·1±0·30	3·1±0·30
Attention to dress and person	3·1±0·56	2·9±1·37	2·9±1·37	2·9±1·22
Psychomotor activity	3·9±0·55	3·8±0·89	3·4±1·48	3·8±0·77
Speech	3·4±0	3·2±1·41	2·9±1·05	3·5±1·48
Toilet behaviour	3·6±1·18	3·7±1·10	3·7±1·10	3·5±1·30

Global ratings ("better", "worse", "no change") were also made by the investigators after their weekly interview with the patients. When drug and placebo periods were compared it was found that there was an excess of "better" ratings in two patients while on the drug and four while on the placebo.

(b) *Toxic Symptoms*

All patients showed minor signs of reserpine intoxication, the commonest being extra-pyramidal symptoms. The incidence of these symptoms, classifying the patients in drug and placebo-treated groups, was expressed as a product of the number of patients and the number of weeks during which the symptoms were shown (Table III). The differences can be seen on inspection to be insignificant. Using the same data but comparing each week on the drug with the third week on the placebo, likewise, no significant difference was found.

TABLE III

Toxic Symptoms

Toxic Symptoms	No. of Patients—Weeks Orphenadrine	Placebo
	Extra-Pyramidal Symptoms	
Rigidity	9	13
Tremor	12	10
Hypersalivation	4	3
Glabellar tapping sign	18	17
Total	43	43
	Vegetative and Cardiovascular Symptoms	
Rhinitis	3	3
Flush syndrome	0	1
Chills	2	2
Giddiness	1	0
Nausea	5	3
Heartburn	1	0
Vomiting	4	5
Pains in extremities	3	0
Disturbance of sleep	3	5
Dry mouth	6	6
Oedematic tendencies	6	5
Urge to urinate	2	1
Total	36	31

The pulse rate was taken at weekly intervals and the mean for each three-week period compared with that for the consecutive period. A difference of greater than 10 per cent. of the first three-week period mean was used as the criterion of change. By this standard in two patients the pulse rate was higher on the drug and in two higher on the placebo. The other six patients showed no change.

In five patients the systolic blood pressure was treated in the same manner as the pulse rate. In four of the five cases there was a difference in the mean readings of less than 10 mm. of mercury and in the fifth a rise of 16·6 mm. of mercury whilst on orphenadrine. These changes were regarded as within the limits of error of the clinical method and without significance.

(c) *Motor Performance Test*

The mean of the times on drug and on placebo taken by nine patients to complete the line drawing test were arranged in rank order for the eighteen three-week periods. Patients above the median were compared with those below it (Table IV) and orphenadrine was not found to produce any change in motor speed as tested.

TABLE IV

Timed Test of Performance

	Orphenadrine	Placebo	Total
Scoring less than the Median time of both groups	4	5	9
Scoring more than the Median time of both groups	5	4	9
Total	9	9	18

The lines themselves were rated for waviness on a three-point scale and the scores of the drug and placebo periods again compared. Seven patients showed no change, two improved on placebo and none while on the drug.

(d) *Effects of the Trial*

In order to show any trend due to the extra attention received by the patients during the trial the doctors' global ratings for the first chronological period were compared with those of the second period regardless of treatment.

Three patients were classified as "better" in each period, suggesting that any effects were either absent or relatively constant.

CONCLUSIONS

Used in doses of 50 mg. t.d.s. no evidence is forthcoming from this small series of patients that the combination of orphenadrine with reserpine (0·5–2 mg. t.d.s.) is of clinical value in mitigating the less severe extra-pyramidal and other side-effects of reserpine. Likewise, no evidence was found for a sedative action or for a significant enhancement of the tranquillizing properties of reserpine as measured by a motor test and behaviour rating scale respectively. The value of orphenadrine in *severe* states of reserpine intoxication has not been tested. Nevertheless, the dosage of reserpine used in this trial is frequently employed in psychiatric practice and in the light of the above evidence it would appear unjustified to combine Orphenadrine with it in a routine fashion. Such a combination, moreover, increases the cost of reserpine medication approximately tenfold.

ACKNOWLEDGMENTS

We wish to thank Dr. John Dawson, Director of Research, for criticism and advice; Sisters Harvey, Mears and McMullen and Miss M. Crouch, M.A.O.T., for help with the ratings; and G. A. Schneidler, Esq., of the Camden Chemical Co., for supplies of "Disipal" and placebo.

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THE ELECTROENCEPHALOGRAM, OBSESSIONAL ILLNESS AND OBSESSIONAL PERSONALITY

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INTRODUCTION

A CLINICAL relationship between obsessional illness and epilepsy is unusual, but the few electroencephalographic (EEG) investigations of obsessional patients which have been published claim a high incidence of abnormal electrical activity. Records of twenty-six neurotic and five schizophrenic patients, all with obsessional symptoms, were examined by Pacella *et al.* (13), who found twenty-two of the thirty-one EEGs to be abnormal. Fourteen showed definite convulsive patterns with frequent 2–4 c.p.s. activity and increased high voltage waves after overbreathing. Rockwell and Simons (14) found only two abnormal records in eleven uncomplicated obsessional neurotics, using Gibb's criteria of normality, but of ten patients classified as psychopathic personalities with obsessional symptoms, all had abnormal EEGs although two were borderline. Their definition of psychopathic personality is not made explicit and the clinical distinction between their two groups is unclear. Jarvie (4) reports a case in which slow activity on hyperventilation in the EEG was associated with phobias and obsessional impulses preceded by a two-year history of episodes of rage.

These findings, if valid, are important and exceptional, because in neurosis in general such a high incidence of EEG abnormality has not been found. The relationship has therefore been investigated again in a series of obsessional patients, all of whom had been admitted to a mental hospital. Such a sample comprises severe and often chronic cases and would be expected to show EEG abnormalities more often and obviously than a less biased sample of obsessional patients in the general population.

Other work suggested that the relationship between the obsessional personality and EEG variables was equally worth investigating. Attempts to correlate EEG variables with personality traits have had limited success (Mundy-Castle, 12; Saul, 16; McAdam *et al.*, 8, 9, 10). Mundy-Castle (12) used the terms primary and secondary functioning in considering personality and related them to high and low alpha frequencies respectively. People with "primary functioning" are said to be quick, impulsive, variable and highly stimulable, while those with "secondary functioning" are slow, cautious and steady. McAdam and Orme (9), working with a group of alcoholics, found an activity-passivity dichotomy corresponding to low and high alpha index, and found a positive correlation between low alpha frequency and high alpha index, thus relating their findings on both EEG and personality grounds to those of Mundy-Castle. Saul *et al.* (16) studying patients in the course of psychoanalysis considered a high alpha index to be associated with a passive, submissive, dependent and receptive attitude; while a low alpha index was associated with a consistent, directed drive to activity. McAdam (10) has suggested that "secondary functioning" would imply a tendency to rumination and perhaps to obsessional thinking. If this is so a series of obsessional patients would be expected to contain a preponderance of records with low alpha frequencies and high alpha indices, or if underlying personality were to be more important than symptoms, this trend would be seen in those patients of markedly obsessional personality.

In the dichotomies described above there is a rough agreement that activity and passivity are important distinguishing features in relation to the type of EEG. It is of interest that Lewis (6), dissatisfied with the conventionally described personality traits of the obsessional, observed two types of personality in chronic severe obsessionals who had had symptoms since childhood. One he described as "submissive, vacillating, uncertain", the other as "obstinate, morose, irritable". It is clear that these two types of personality can be regarded as closely connected with the dichotomies just discussed.

To summarize, it was expected from previous findings that a group of obsessional in-patients would show a high incidence of EEG abnormalities, and would show a tendency to high alpha index, or that those with markedly obsessional personalities would show such a tendency. Those patients with the obstinate, morose, irritable traits described by Lewis should have a low alpha index and those in his second group (submissive, vacillating, uncertain) should have a high alpha index.

METHOD

The thirty subjects were in-patients showing predominantly obsessional symptomatology: obsessional states in the broadest sense. The absence of out-patients implies that the cases were of some severity; in fact, many were chronic. They were divided into five diagnostic categories:

1. Obsessional-compulsive neurosis. A classical or nuclear group, typifying the textbook description and showing obsessional and compulsive symptoms in a sustained symptom complex with no evidence of psychotic disturbance of thought or mood, organic nervous disease or other neurotic symptoms. Cases in any way atypical were automatically and strictly excluded from this group.
2. Obsessional-ruminative neurosis. Those cases with predominantly phobic and ruminative symptoms with minimal or absent motor signs and no psychotic or organic signs. As in (1) atypical cases were excluded.
3. Doubtfully schizophrenic. Those cases in which symptoms suggestive of schizophrenia were found in combination with obsessional symptoms. Many such diagnostic problems arise in the obsessional states found in mental hospital practice and the diagnosis is only clarified by the passage of time. The category has a precedent in the work of Rüdin (15).
4. With affective features. Those cases in which obsessional symptoms were associated with a sustained mood change, invariably depressive. The category was designed to explore the borderland between obsessional illness and endogenous depression: the "endogenous obsessional neurosis" of Mayer-Gross *et al.* (7).

5. Miscellaneous. This group contained one patient with epilepsy, one with arteriosclerotic dementia and one with hysterical symptoms.

Twenty-two of the patients belonged to groups 1 and 2 and were therefore typical cases of obsessional neurosis, while the remaining eight were atypical.

In assessing obsessional personality seven features mentioned by Lewis (6) as characteristic of the obsessional personality were taken into account: excessive cleanliness, orderliness, pedantry, conscientiousness, uncertainty, inconclusive thinking and acting, and fondness for collecting things. "Marked obsessional traits" represent the presence of five or more of these, "slight" the presence of two to four, and "not obsessional" less than two. The two clusters of traits described by Lewis were scored as present or not applicable.

The recordings were made on a standard 8-channel machine, the only refinement being the use of a band-pass filter (Morris and Dawe, 11) to obtain a more accurate measurement of alpha activity than would have been possible by visual analysis alone. Microvoltage, frequency and distribution were estimated for slow activity (delta—less than 4 c.p.s., and theta—4–7 c.p.s.), alpha activity (8–13 c.p.s.) and fast activity (beta—14–30 c.p.s.). Using the band-pass filter an estimate was made of alpha index. This index expresses as a percentage the duration of time in which alpha activity is apparent; an index of 100 would signify continuous alpha and an index of zero that no alpha activity was visible.

The clinical and electroencephalographic investigations were made independently by the authors and the findings of one were not known to the other until the series was completed.

RESULTS

1. *EEG Abnormalities*

Twenty-three of the 30 records were within normal limits (Table I). In the three cases termed mildly dysrhythmic the abnormality in each case was the appearance of slow, generalized dysrhythmic bursts on hyperventilation. These were all minimal and were considered to be borderline.

TABLE I

Incidence of EEG Abnormalities

Diagnostic Group	Normal	Mildly Dysrhythmic	Abnormal	Total
Compulsive neurosis ..	15	2	1	18
Ruminative neurosis ..	3	1	0	4
Doubtfully schizophrenic ..	0	0	1	1
Affective	2	0	0	2
Miscellaneous	3	0	2	5
Total	23	3	4	30

In four cases definite abnormalities were found. In the miscellaneous group, one case was known to suffer from major epilepsy and the other showed signs of moderate arteriosclerotic dementia clinically and on psychological testing. The EEG of the epileptic unexpectedly showed a petit mal variant, that of the arteriosclerotic patient an abnormal amount of generalized slow activity and slowing of all frequencies, consistent with an organic dementia.

The patient in the doubtfully schizophrenic group was obviously schizophrenic at follow-up two years later. The EEG showed one generalized synchronous burst of "sharp" waves in the resting record. There was no clinical evidence and no family history of epilepsy.

Among the typical patients in the first two diagnostic groups only one definitely abnormal EEG was found. The patient concerned, a woman of 43, had a long-standing obsessional compulsive neurosis which had its onset in adolescence and had run an unremitting course. The only atypical feature was her considerable irritability which frequently led to outbursts of temper when her rituals were interfered with in any way. The EEG showed several bursts of synchronous, generalized delta waves. Again there was no clinical or family history of epilepsy. The history and EEG findings are reminiscent of the case described by Jarvie (4).

2. *Alpha Index, Diagnostic Grouping and Personality Traits*

In Table II "high index" indicates an index between 55 and 100; "low index" one between 0 and 45. Two cases in which the index was between 45 and 55 have been omitted. In the group as a whole the results are quite contrary to hypothesis as low index cases are more common than high index cases. This finding is more pronounced in the typical compulsive neurotics.

TABLE II
Diagnostic Group and Alpha Index

Diagnostic Group	Alpha Index High	Alpha Index Low
Compulsive neurosis	5	12
Ruminative neurosis	2	1
Doubtfully schizophrenic	1	0
Affective	3	2
Miscellaneous	1	1
Total	12	16

In considering the relationship between personality traits and alpha index only those with normal records were included and the two cases with alpha index between 45 and 55 were again omitted. The results using all 30 cases and records do not, in any case, differ from those found with this more careful selection.

Inspection of Table III shows no correlation between obsessional personality and high or low alpha index, but in the two types of Lewis there is a tendency for the first to have a low alpha index and the second a high index, both as predicted. The correlation is small (phi-coefficient=0·34) and does not reach statistical significance (p=0·2).

TABLE III
Personality and Alpha Index

	Alpha Index High	Alpha Index Low
A. Obsessional Personality:		
Marked	4	5
Slight	4	4
Not present	2	2
B. Lewis Types (6):		
Obstinate, morose, irritable	2	5
Submissive, vacillating, uncertain	5	3
Neither applicable	3	3

Attempts to correlate personality factors with other EEG variables, such as the presence and amount of slow and fast activity, gave negative results.

Discussion

Borderline and definite abnormalities were found in only seven of the thirty patients and if the borderline cases are rejected the number of definitely abnormal records is four or 13 per cent. of the group. To arrive at a true incidence of EEG abnormality in typical cases of obsessional neurosis it is necessary to exclude the atypical diagnostic categories, where the abnormalities were associated with clinical dementia, epilepsy and schizophrenia. There remains one abnormal record in the 22 typical cases of compulsive and ruminative neurosis, despite the fact that all these patients had symptoms severe enough to require hospital treatment. This figure suggests that the incidence of electrical abnormality in obsessional states is no different from that in other neurotics or indeed in the normal population (Lennox, Gibbs and Gibbs, 5; Hill and Watterson, 3; Williams, 17).

Our findings contradict those of the two previous series and it is pertinent to seek other evidence for or against them. No figures for the frequency of the association between epilepsy and obsessional illness have been traced. Garmany (2) reported a single case and Brickner (1) two unusual histories. In the first an epileptic's seizures were ushered in by phobias, and in the second compulsive swallowing movements were noted in the post-ictal period in a patient who had suffered from compulsive swallowing twenty years earlier. These few reports are the sole evidence for a clinical association. One of us (I.M.I.) in a series of 105 obsessional states has found only two cases of epilepsy (both grand mal). In neither was any connection between the epilepsy and the obsessional symptoms apparent and the association in each case seemed to be a chance one. The low incidence, less than 2 per cent., which compares with an incidence of approximately 0·5 per cent. in the general population, also suggests that the association is a chance one. These two observations lend support to the negative EEG findings in the present group of patients.

No connection has been found between the EEG variable chosen (alpha index) and either obsessional illness or the conventionally described obsessional personality. The suggestion that "secondary functioning" would imply a tendency to rumination and obsessional ways of thinking is unfounded, the results being contrary to those expected from this argument. The two types of personality formulated by Lewis (6), roughly corresponding to an activity-passivity division, did tend to have the predicted types of alpha index. Our results imply that specifically obsessional traits and symptoms have no relation to EEG variables but that further investigations of personality in relation to electroencephalography should continue to explore activity-passivity differences.

Summary

1. Four out of 30 patients with predominantly obsessional symptoms had definite EEG abnormalities; when atypical cases were excluded only one of twenty-two typical cases of obsessional neurosis had an abnormal record.

2. No correlations were found between alpha index and either obsessional symptoms or traits, but active personalities tended to have a low alpha index and passive personalities a high index.

3. The relationship between obsessional illness and both epilepsy and EEG abnormality is considered to be a chance one.

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THE EFFECT OF ELECTRO-CONVULSIVE THERAPY ON SPINAL FLUID CONSTITUENTS

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During the course of an investigation of the effectiveness of various components of electric convulsive therapy in the treatment of hospitalized psychiatric patients (Brill *et al.*, 1957, 1959) observations were made on the spinal fluid concentrations of cations and total protein before and after treatment. The possibility existed that alterations in brain function and structure (which are believed by many to occur during a course of electro-convulsive treatment, and to be responsible for improvement in patients receiving such treatment) might be associated with, or reflected by measurable changes in the cerebral spinal fluid.

Although changes in blood serum following E.C.T. have been observed, there has been a surprising lack of studies on the cerebral spinal fluid. In a paper published in 1945, Spiegel-Adolf *et al.* (10), using dogs, measured the concentration of potassium, inorganic phosphorus, and total protein before and after electrically induced convulsions. The animals were given from two to fifteen shocks. Measurements were made from one-half hour to three days after the last seizure. The data obtained indicated that there was a significant rise in potassium and phosphorus values within one hour after the last seizure and a return toward pre-treatment levels in one to three hours. No change in the total protein concentration of the spinal fluid was observed. In an earlier study, Katzenelbogen (6), using metrazol-induced convulsions in a sample of psychiatric patients in St. Elizabeth's Hospital, measured a number of constituents in the spinal fluid and found no increase in Na^+, K^+, or Ca^{++} following the treatment. However, the time of collection of samples following the treatment was not specifically given.

At the time both these studies were done, the methods available for the measurements of Na^+, K^+, Ca^{++}, were time-consuming and difficult, possibly accounting for the small number of reports of such studies on the spinal fluid. The development of flame-photometric techniques has provided a convenient and accurate method for determining the concentration of these cations. In 1951, making use of this technique, Shaw and Holley (9) examined the cerebral spinal fluids of 100 hospitalized patients without any evidence of organic or functional disease of the nervous system for their levels of sodium and potassium. The mean value obtained for sodium was 142 meq. with a range from 134 to 152 meq. The mean for potassium was 2·88 meq. with a range of 2·50 to 3·65 meq.

Katzenelbogen (5) summarized the earlier literature, and a recalculation of the data presented by him indicates that cerebral spinal fluid sodium levels in a population of 64 normals obtained by different investigators using different techniques ranged from 112 meq. to 166 meq. With respect to potassium, the summarized data, recalculated, show a range of 2·56 meq. to 4·32 meq. in 63 normal subjects. In his own study, Katzenelbogen found a range of 3·28 to 3·99 meq. of potassium in the spinal fluid of 12 psychotic patients. He also summarized the data on calcium levels in the cerebral spinal fluid. The values reported on subjects with no known functional or organic disease of the nervous system ranged from 4·1 to 6·1 mg. per cent., while the levels found by Katzenelbogen in 50 patients with schizophrenic and manic-depressive disorders ranged from 4·1 to 5·3 mg. per cent.

The range of total protein levels in the spinal fluid was found to be from 6 mg. per cent. to 100 mg. per cent., according to Neel (7) who summarized the data obtained from various workers from 1895 to 1938. Peterson (8) using a turbidimetric method on a general hospital patient population reports that on 257 spinal fluids examined which had essentially normal cell counts, normal globulin levels and normal colloidal gold curves, 94 patients had 40 mg. per cent. or less, 109 had 40–60 mg. per cent., 49 had 60–100 mg. per cent., and only 5 had over 100 mg. per cent. Katzenelbogen (5) in a study of the total protein levels in the spinal fluid of a mixed group of psychotic patients finds that 89 per cent. of his cases fell in the range of 16–45 mg. per cent., 4 per cent. in the 10–15 mg. per cent. range, and 7 per cent. in the 46–80 mg. per cent. range. In a study of 1,281 patients of the "dementia praecox group", Breutsch *et al.* (1) found that the range of total protein in the cerebral spinal fluid was 46–166 mg. per cent. with only four patients over 100 mg. per cent. The remaining patients varied between 46–99 mg. per cent.

In the present study the subjects were 96 male psychiatric patients from the Brentwood Veterans Administration Neuropsychiatric Hospital in Los Angeles, for whom shock treatment had been prescribed. None had had shock treatment in the preceding 9 months. All were male veterans. Sixty-six were suffering from chronic schizophrenic reactions and 30 from schizo-affective disorders or depressive reactions. The illness in a majority of the patients was characterized by exacerbations and remissions and many had received electroshock treatment previously with beneficial effect. The patients' ages ranged from 18 to 68 with a mean of 35. Patients with recognized organic disease of the central nervous system were excluded.

The 96 subjects were randomly assigned to one of the five treatment groups; regular E.C.T., E.C.T. plus anectine, E.C.T. plus pentothal, pentothal alone, and nitrous oxide alone. The present report is concerned with the spinal fluid concentration of cations and total protein in the entire sample rather than with the five sub-samples. A course of 20 treatments was administered to each patient, given at the rate of three times a week. Spinal fluid determinations were made on each subject prior to the beginning of treatment, two weeks following the last treatment, and again one month following the last treatment*.

The results obtained in the present study for the pre- and 1 month post-treatment levels of sodium, potassium, calcium, and total protein in the cerebral spinal fluid are summarized in Table I. (The mean and range of these constituents measured 2 weeks after completion of treatment were substantially the same as those obtained after 5 weeks and are therefore not included in the table.)

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* Because it was not possible to obtain every sample on every patient, the number of subjects in each category varied as indicated in the text.

TABLE I

Concentration of Cations and Total Protein in C.S.F. of a Sample of Psychotic Patients

		Pre-Treatment			Post-Treatment		
		$\bar{X}$	Range of Values	S.D.	$\bar{X}$	Range of Values	S.D.
Meq. Na+	(a)	152	138–166	5·55	153	142–174	6·30
Meq. K+	(a)	3·1	2·6–3·8	·233	3·1	2·4–4·8	·389
Mg. % Ca++	(a)	5·4	3·8–8·6	1·14	5·2	2·0–9·0	1·22
Mg. % total protein	(b)	39	8–84	13·2	41	12–110	15·6

a = Method of Kingsley, G. R., and Schaffert, R. R., *Analytic Chem.*, 1953, **25,** 1738.
b = Method of Kingsley, G. R., and Getchell, G., *J. Biol. Chem.*, 1957, **225,** 545.

(a) *Sodium and Potassium.* The data indicate that there is no change in the mean concentration of these ions between the pre-treatment levels and those observed one month following treatment. There appeared to be no shift in the range of values obtained before and after treatment in these patients. The range of values observed in the spinal fluid of these psychotic subjects is similar to that observed in the literature for "normal subjects" (5, 7, 8, 9).

The effect of convulsive or non-convulsive treatment upon the distributions of sodium and potassium levels as well as the relationship of these levels to the response to treatment (i.e. improvement or non-improvement) is shown in Figures 1 and 2. It can be clearly seen that there is no significant difference between the distributions of spinal fluid levels of sodium and

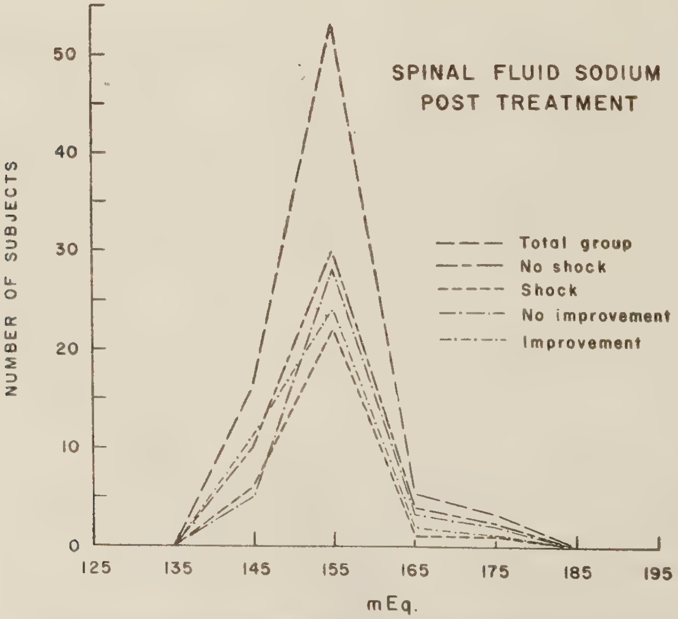

FIG. 1.—C.S.F. sodium levels in patients five weeks after termination of treatment.

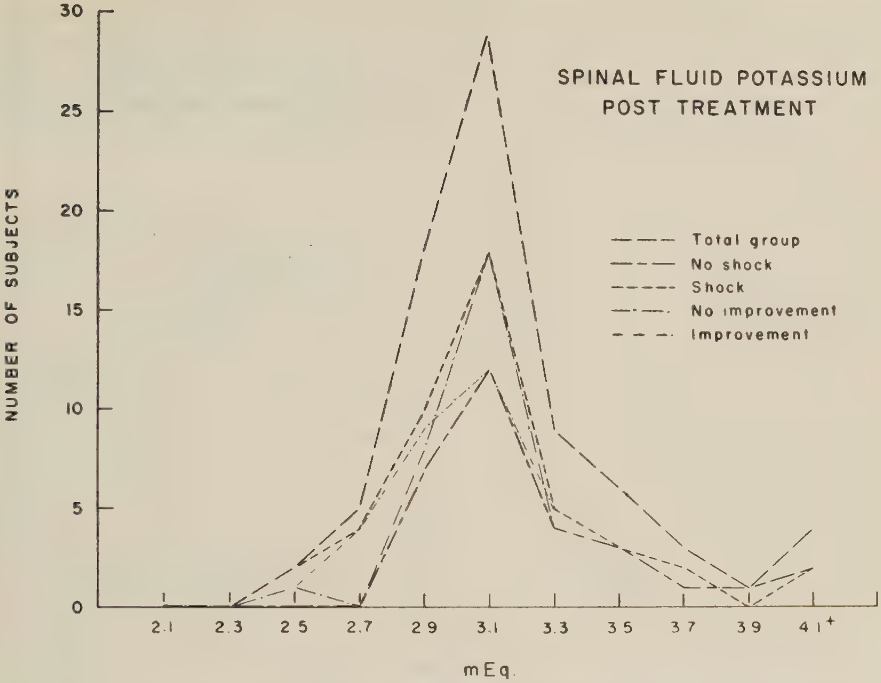

FIG. 2.—C.S.F. potassium levels in patients five weeks after termination of treatment.

potassium in those patients who received one of 3 types of electroshock treatment and those who received one of the other forms of treatment (i.e. repeated administration of pentothal or nitrous oxide). Furthermore, the similarity of the distribution curves of those patients who improved (irrespective of type of treatment) and of those showing no improvement strongly suggests that no relationship exists between spinal fluid sodium and potassium and the clinical state of the patient after treatment. It had been previously shown that clinical response to treatment was unrelated to the pre-treatment values of sodium and potassium in the spinal fluid (4).

(b) *Calcium.* Just as in the case of the other cations, the spinal fluid calcium levels do not show any significant change in their mean or range whether determined before treatment or 1 month after treatment. Among the pre-treatment values, only 4 patients of the 90 studied had calcium levels above 6·0 mg. per cent. With respect to the post-treatment data, again only 4 patients out of 73 had values greater than 6·0 mg. per cent. while only 3 patients, with previously higher levels, had levels less than 3·8 mg. per cent. The relationship of post-treatment calcium levels to improvement and to type of treatment is shown in Figure 3. When the pre-treatment spinal fluid calcium levels of patients who improved were compared with those who did not improve, it was found that the unimproved group tended to show higher initial levels.

(c) *Total Protein.* The data from Table I indicate the similarity of means and ranges of total protein levels in the spinal fluid when determined before treatment and 1 month after treatment. There was only one value (8 mg. per cent.) below 20 mg. per cent. in the 88 patients studied prior to treatment, and only 8 values that were over 55 mg. per cent. There was no relationship between age or EEG abnormality and level of spinal fluid protein. One month after treatment, out of a total of 74 determinations there were only two with

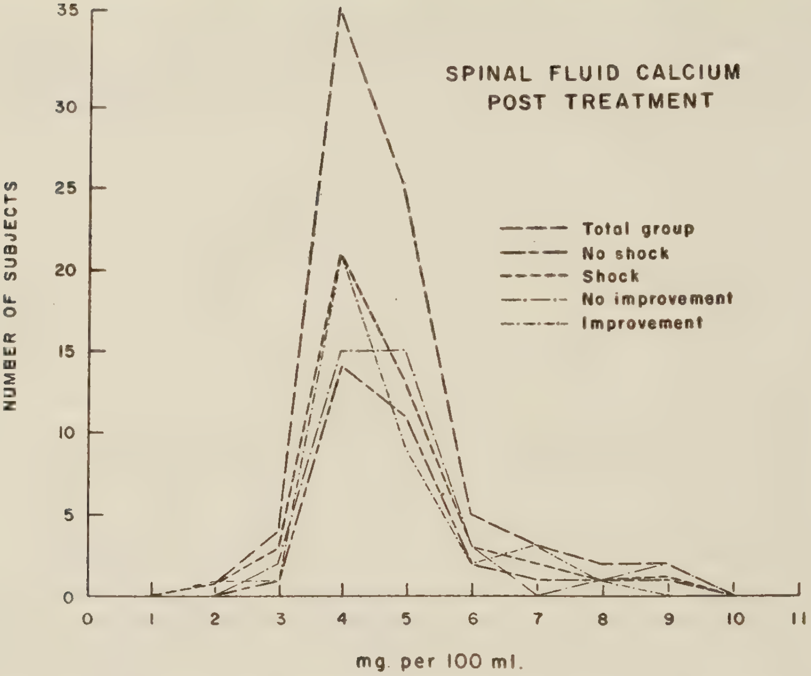

FIG. 3.—C.S.F. calcium levels in patients five weeks after termination of treatment.

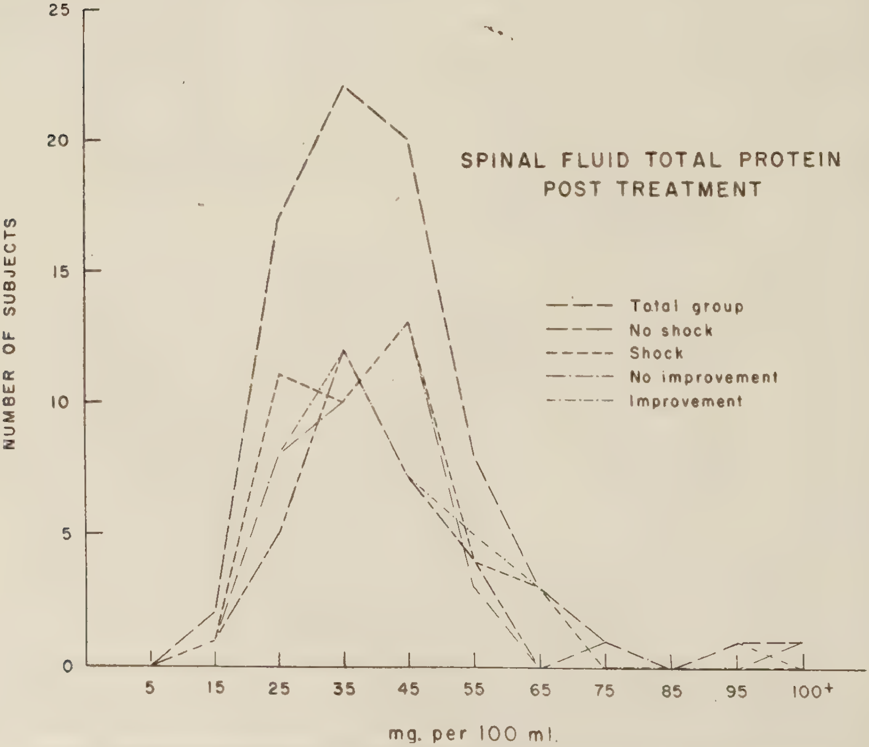

FIG. 4.—C.S.F. protein levels in patients five weeks after termination of treatment.

values (12 and 19 mg. per cent.) under 20 mg. per cent., and eight with values over 55 mg. per cent. The relationship of spinal fluid total protein to improvement and to type of treatment is illustrated in Figure 4. The coincidence of the distribution curves clearly indicates that neither the type of treatment, nor the response to it, is reflected in the level of spinal fluid total protein.

DISCUSSION

Although changes taking place in the concentration of these and other substances in the spinal fluid *immediately* following an electrically induced convulsion have been described in animals and in humans (Spiegel-Adolf, 1948) the above data would indicate that by the end of the 5th week following cessation of treatment, the concentrations of these substances apparently have returned to pre-treatment levels.

Statistical analysis of the concentrations of sodium, potassium, calcium and total protein in the spinal fluid as related to improvement of the patient or to the mode of treatment of the patient revealed that only the pre-treatment level of spinal fluid calcium showed a relationship with improvement of the patient (4). A total of twenty biochemical variables in serum and the spinal fluid were statistically analysed, and since only this one parameter of the spinal fluid constituents was found to have a relationship, it is possible that this finding could appear by chance alone. Of course, it is possible that the overall determination of these ions and protein in spinal fluid may not reflect transient or permanent localized changes in particular areas of the brain which could influence the activity of neural nets and secondarily the clinical condition of the patients.

Our data cannot answer the question concerning the production of any persistent physical alteration in the brains of these patients whether treated by shock or non-shock methods. What is clear however, is that if changes did occur they were not reflected in changes in sodium, potassium, calcium, or total protein levels in the spinal fluid.

The rather broad ranges of values for calcium and total protein found in this patient sample are not appreciably different from those which have previously been described for normal subjects. The fact that such broad ranges occur is in itself of interest and as yet without adequate explanation.

SUMMARY AND CONCLUSION

1. The distributions of values of sodium, potassium, calcium, and total protein in a sample of 96 psychotic patients are not different from reported distributions found in non-psychotic populations.

2. The response to treatment seems unrelated to the pre-treatment values of these elements of the spinal fluid.

3. Electro-convulsive treatment does not result in any significant change in these components of the spinal fluid when measured 1 month after completion of a course of treatment.

4. Change in clinical condition does not appear to be associated with any change in these constituents of the spinal fluid.

ACKNOWLEDGMENTS

The authors wish to thank Mr. Lloyd Dowdell, Mr. Raymond Wallace, Mrs. LaVerne Keesling, and Miss Marie Brady for their technical help. We are most grateful to Dr. Wilfred J. Dixon for his helpful suggestions with the statistical analysis of the data.

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TREATMENT OF CHRONIC PSYCHOTICS WITH B.A.S.

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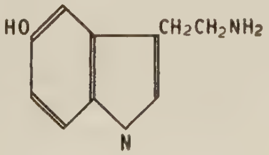
In the past few years papers have appeared in the U.S.A. and in Europe which discuss the role played by 5 hydroxy-tryptamine (serotonin) in cerebral metabolism, both in health and disease. The aim of this paper is to report a trial of a benzyl analogue of serotonin, a serotonin antagonist, and to shed some light upon its possible side-effects.

Reserpine is said to reduce the concentration of serotonin in the tissues, possibly by displacing the latter from its receptors. Serotonin causes the smooth muscle in arteries and viscera to contract, hence it may be an aetiological factor in the production of hypertension. Only about 1 per cent. of the serotonin content is found in the brain, most being found in the spleen and in the tissues forming the gastro-intestinal tract. Patients suffering from a malignant tumour of the chromaffin cells called carcinoid disease often show high levels of blood serotonin, for which reason Davies and Rimington (1) and other workers have tried serotonin antagonists in cases of carcinoid disease. In one such case B.A.S. was used but the condition was controlled only to a very limited extent. An incidental but highly interesting observation made at the time was that the patient, previously depressed, anxious and often tearful, became placid, cheerful and, in the fullest sense of the word, "tranquillized" while on the drug.

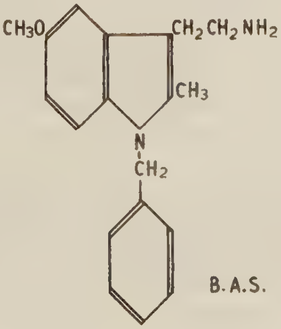
This observation, together with a tentative hypothesis that B.A.S. might act by blocking the action of serotonin in cerebral metabolism, led the author to undertake a small-scale trial with the drug on a limited number of female psychotic patients, to compare the efficacy of the drug with chlorpromazine in the management of agitation, restlessness and anxiety.

B.A.S.

B.A.S. was first synthesized by Shaw and Woolley (2) who showed this compound, 1-benzyl-2-5-dimethylserotonin, to be a very potent anti-metabolite of serotonin both *in vitro* and *in vivo*.



SEROTONIN



B.A.S.

B.A.S. has been administered to man for the treatment of hypertension by Wilkins (3, 4) and very recently, while the trial described herein was in progress, a paper has been published in the U.S.A. by Rudy (5) showing that it has been employed for the treatment of schizophrenic patients.

METHOD

Initially twenty female psychotic patients were selected for the trial, all of whom were considered to have a poor prognosis. Most exhibited behaviour disorders, warranting regular maintenance E.C.T. in order to render them manageable.

All the patients had previously had a course of chlorpromazine. This was useful since any new drug should be compared with existing preparations and chlorpromazine was deemed a suitable yardstick for the present purposes.

All medication was discontinued for a period of 4 weeks to avoid confusion by overlap of chlorpromazine treatment. This treatment-free period was followed in all cases by 4 weeks' therapy with B.A.S. As will be seen, this part of the trial was not completed by all patients due to marked side-effects arising in some cases. After the trial period another treatment-free interval of 4 weeks was reinstated. This was done in order to detect any after-effects of treatment, and it was also hoped to obtain some idea of how long a remission would last. After this 4-week period free of treatment patients were replaced on chlorpromazine if necessary.

The trial group consisted of: 7 schizophrenics, 6 paraphrenics, 1 schizophrenic reaction superimposed upon a psychopathic personality, 1 melancholic, 2 epileptic psychotics, 2 manic-depressive psychotics and 1 mental defective exhibiting behaviour disorders.

The patients were all nursed in the same ward and were fully and frequently observed by the nursing staff. All patients attended the occupational therapy department and frequent reports were obtained on the patients' progress from the therapists. Before the trial commenced full physical and psychiatric examinations were carried out and recorded, together with a preliminary blood count.

Blood pressures were recorded daily at the same time of day, and at weekly intervals body weights were noted.

B.A.S. was supplied in the form of 50 mg. tablets, scored for division into 25 mg. segments. All patients commenced treatment with 50 mg. t.d.s. Some patients were withdrawn from the trial due to serious side-effects after a total dosage of 300 mg. The remainder had their dosage reduced to 25 mg. t.d.s. and then slowly increased to 50 mg. t.d.s. over a period of 2 weeks.

In 6 cases B.A.S. had to be discontinued due to profound side-effects and in one case a patient was transferred to another institution. The 7 cases who fell by the wayside were replaced by a further 7 suitable cases. The assessment was made on the psychiatric condition of the patient, the following factors being considered in all cases:

(*a*) Florid symptoms; hallucinations, delusions, etc.

(*b*) Behaviour; violence, controllability, submissiveness, etc.

(*c*) Accessibility, including degree of retardation.

(*d*) Affective response.

For the purposes of recording, however, a simple numerical record was made as follows:

1. Recovery.
2. Much improved.
3. Improved.
4. Unimproved.
5. Deterioration in the psychiatric condition.

All patients when being treated with chlorpromazine were assessed as category (4).

After completion of the period of treatment with B.A.S.:

2 cases were placed in category 1
3 cases were placed in category 2
3 cases were placed in category 3
13 cases were placed in category 4
5 cases were placed in category 5

Of the two cases who were up-graded as the result of treatment with B.A.S. to category 1, one was returned to voluntary status and discharged, her condition (paranoid schizophrenia) having remitted; the other who had previously been acutely suicidal and auditorily hallucinated, was able to go out shopping, and allowed leave of absence. After 3 months she was placed on a small maintenance dose (25 mg. t.d.s.) and subsequently required only occasional E.C.T. to maintain her improvement.

One patient, a depressive, requested resumption of treatment with B.A.S. as it improved her condition. She was maintained on 25 mg. t.d.s., and was placed in category 2. In the 8 cases who were improved by treatment with B.A.S. (i.e. categories 1, 2 and 3) it was particularly noticeable that the florid symptoms had disappeared, and insight was gained into the nature of these symptoms.

All 8 cases, because of their improvement, were not replaced on to chlorpromazine during the last period of the trial. Those cases who deteriorated with B.A.S. were replaced after the 4-week treatment-free interval on to chlorpromazine therapy, and dramatic improvement in their condition was seen, but never much beyond their original condition (i.e. category 4).

SIDE-EFFECTS

Side-effects resulting from the use of B.A.S. were considerable. In 6 patients they were of such an order that after 6 doses, a total of 300 mg., the drug had to be discontinued and the trial abandoned.

Chiefly amongst these severe side-effects were:

1. *Vertigo*. Six patients complained of profound dizziness to the extent that walking unaided was impossible.
2. *Ataxia*. Four of these patients showed a profoundly ataxic gait, with gross tremor of the hands. Co-ordination of body movements was disturbed, the patients being unable to hold a cup or spoon for feeding. These symptoms occurred after 6 doses, a total of 300 mg. having been administered. Cessation of treatment was followed by a slow recovery, complete in 7 days after stopping the drug.

3. *Abdominal Pain.* Severe and cramp-like abdominal pain occurred in 4 of the 6 cases, accompanied by—
4. *Vomiting*, in 3 cases, which persisted for 2 days after withdrawal of the drug.
5. *Circulatory Collapse.* Occurred in 2 cases associated with hypotension. In the first case the blood pressure fell drastically, the patient became pale, cold, clammy and cyanosed. For 3 days afterwards she was confused, restless, incontinent of urine and faeces, the condition returning to the patient's normal state at the end of this time. In the second case the blood pressure fell, the patient was shocked, pale, sweating profusely and the pulse was impalpable. The lips were cyanosed and gross dysarthria was present. She recovered slowly over 14 days. In both these cases a total of 300 mg. B.A.S. had been given over a period of 2 days and treatment had to be discontinued.
6. *Bradycardia.* A marked and persistent fall in pulse rate during treatment was noticed in one patient (from 72–54) and this was associated with the usual hypotension. This patient also complained of giddiness but recovered slowly after a period of 3 days after withdrawing B.A.S.

Other side-effects associated with B.A.S. were:

7. *Weight Loss.* This occurred in every case which was treated with B.A.S. except one. The weight loss varied from 1 pound–15 pounds, the average weight loss per patient being 7 pounds.
8. *Hypotension*, to a small degree was noticed in every case. The average overall blood pressure during treatment with B.A.S. was 100/78. The systolic blood pressure fell 20–30 mm. of mercury in many cases, but once treatment was maintained, patients appeared to suffer no ill effects from the hypotension. Only when circulatory collapse ensued as has been described in the above two cases was it found necessary to withdraw B.A.S.
9. *Sedation.* Sleepiness was rarely encountered. Only in one case was it noted to any excessive degree.

DISCUSSION

The results obtained on the whole with B.A.S. in this group totalling 26 chronic psychotic female patients of middle age were disappointing. In 8 cases a satisfactory response was obtained, but in 18 cases the response was negative. Side-effects when they occurred were dramatic and alarming, both to the patient and the clinician. The results of this trial make it tempting to suggest that there might be two opposing conditions both leading to psychoses. In one state one can postulate an excess of serotonin in the cerebral tissues and in the other condition a deficiency of the substance. Because of the paucity of knowledge relating to the distribution of serotonin in free and combined forms in the brain it is pointless to speculate whether these serotonin values would be absolute or relative values, i.e. whether there is a true excess of serotonin or whether there is inadequate binding of the substance.

On clinical grounds it is impossible to forecast which patients will do well on B.A.S. and which will deteriorate. In the absence of any means for measuring brain serotonin levels one wonders whether measurements of blood serotonin levels (bound and free) would in any way help in forecasting which patients may warrant a trial with B.A.S. It is just possible that such levels might reflect the state of affairs in the brain although there is no reason to assume such a direct relationship. It is worthy of note in this connection that those patients who improved on treatment with the drug showed no evidence of serious side-effects developing.

SUMMARY

Twenty-six chronic psychotic female patients, all nursed in the same ward and whose response to chlorpromazine therapy had been ascertained, were subjected to a trial of a serotonin antagonist, B.A.S. (1-benzyl-2-5-dimethyl-serotonin) in order to ascertain whether this drug should have a place amongst psychotropic therapeutic agents. B.A.S. gave rise to a degree of improvement in 8 cases which was satisfactory, but side-effects, mainly of hypotension, loss of weight, ataxia, and abdominal pain, were frequently seen in those patients whose psychological condition did not improve.

ACKNOWLEDGMENTS

I wish to thank Dr. A. C. Sinclair, Medical Superintendent of the Herrison Hospital, Dorchester, for permission to publish this paper, the nursing and occupational therapy staff for their interest and co-operation, and Dr. R. A. Miley and British Schering Limited for their unfailing help and for the supply of B.A.S. tablets.

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PHENELZINE ("NARDIL") IN THE TREATMENT OF ENDOGENOUS DEPRESSION

By

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and

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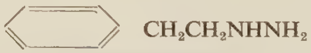
> "Let him take a course of chymistry, or a course of rope dancing or a course of anything he is inclined at the time."
>
> (Boswell's *Life of Johnson*) (1)

To many minds there can be but little change in the treatment of depression since Johnson prescribed these remedies in 1776. Indeed the place of chemistry is now prominent, although its application is apparently more important to the patient than its study. It is believed that an enzyme, mono-amine oxidase, found in cerebral tissues, plays a part in the genesis of depression. Amphetamine inhibits the destruction of adrenaline by amine oxidase (McIlwain, 6) and amphetamine is of value in the treatment of mild depression (Guttmann and Sargant, 5). Another substance is 5-hydroxytryptamine, or serotonin, which is said to excite cerebral neurones briefly between its liberation and destruction; it is a cerebral vasoconstrictor and is destroyed rapidly by amine oxidase (McIlwain, 6). Iproniazid (Marsilid) is a drug which inhibits amine oxidase and has been used in the treatment of depression (West and Dally, 10). Its central actions are considered to be similar to those of 5-hydroxytryptamine. Recently, Chessin (3) has described yet another amine oxidase inhibitor, phenelzine, which is the study of this paper.



PHENELZINE
β-phenyl ethyl hydrazine

It is believed to be more rapid in action than iproniazid and it is said to act preferentially on cerebral tissues rather than on the liver, whereas iproniazid inhibits amine oxidase equally in the brain and in the liver.

METHOD

Thirty-four female patients were selected for the trial. Their ages ranged from 26 to 77 (mean age 57). They had suffered from recurrent attacks of endogenous depression for an average period of eight years. All had had E.C.T. previously. A sheet bearing the following fourteen items was scored weekly for each patient on a four-point scale (0 to 3). The items were as follows: feelings of depression, suicidal ideas, ideas of unworthiness, retardation, ideas of reference, loss of appetite, constipation, somatic delusions, inability to sleep, early waking, agitation, daily mood swing, loss of weight and self-neglect. The patients were selected for two groups, A and B, by tossing a coin. A double-blind cross-over trial was carried out so that each group formed its own control. Group A was given phenelzine, 15 mg. t.i.d. for two weeks and group B was given a placebo of identical appearance t.i.d. for the same period. At the end of two weeks patients in group A were given the placebo and those in group B were given phenelzine for a further two weeks. For the third and last period of two weeks all patients were given phenelzine. It was felt reasonable to limit the trial to a relatively short period since depression can remit spontaneously in a few weeks and existing treatments for depression are often effective fairly rapidly. The patients were seen at the same time each week by both investigators, but the patients of D.S. were assessed by J.T.H. and vice-versa. The trial was controlled by the hospital pharmacist and none of the medical or nursing staff knew which of the patients were having the drug and which the placebo.

RESULTS

An analysis of the item sheets before and after the trial gave the following results, which includes the effect of both drug and placebo.

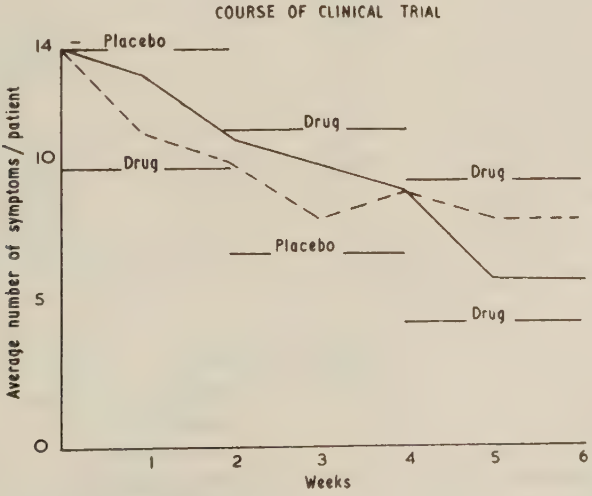
TABLE I

Type of Response	Percentage Remission of Symptoms	No. of Patients
Greatly improved	75–100	13 (38%)
Moderately improved	50–75	7 (20%)
Slightly improved	25–50	7 (20%)
Little change	0–25	2 (5%)
Made worse	—	5 (14%)

Nine patients (26 per cent.) of the group were discharged from hospital after treatment.

A more detailed analysis of the remission rate produced the following findings:

A. Figure 1.



The interrupted line represents Group A.
The unbroken line represents Group B.

FIG. 1.—Course of the clinical trial.

B. Analysis of the remission rate of individual symptoms after both drug and placebo gave the following results which fell into three main categories:

TABLE II

Percentage Remission	Symptoms	Percentage Remission	Symptoms	Percentage Remission	Symptoms
75	suicidal ideas	61	feelings of depression	41	inability to sleep
74	ideas of reference	59	ideas of unworthiness	39	early waking
73	daily mood swing	56	poor appetite	32	agitation
72	retardation	55	constipation	24	somatic delusions
71	weight loss	50	self neglect		

C. Figure 2.

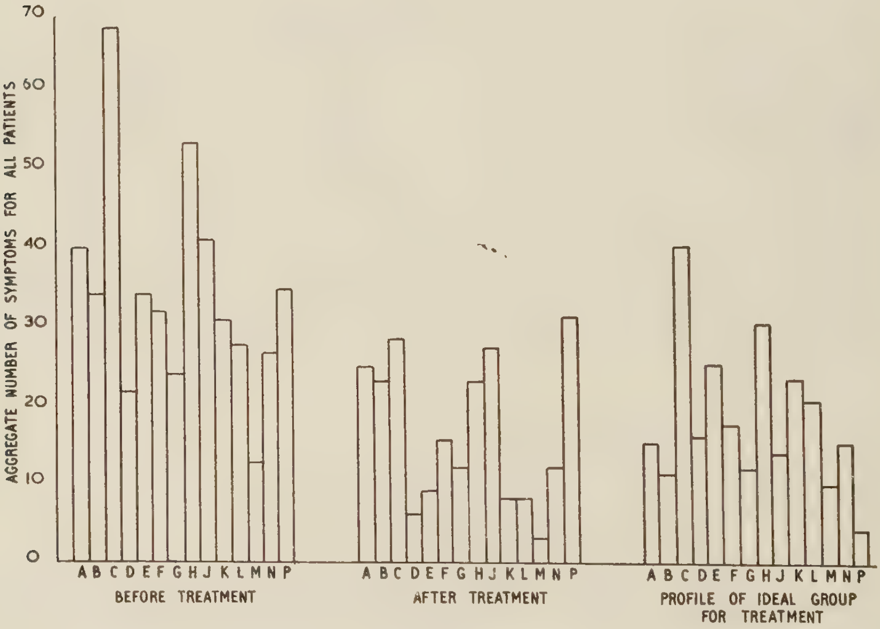


FIG. 2.—Histogram showing profiles of total symptoms before and after clinical trial, and also the profile of the type of depression most likely to respond to this form of treatment.

EXPLANATION OF SYMBOLS

A. Inability to sleep.
B. Early waking.
C. Feelings of depression.
D. Ideas of reference.
E. Retardation.
F. Loss of appetite.
G. Self neglect.
H. Ideas of unworthiness.
J. Agitation.
K. Suicidal ideas.
L. Loss of weight.
M. Daily mood swing.
N. Constipation.
P. Somatic delusions.

D. Figure 3.

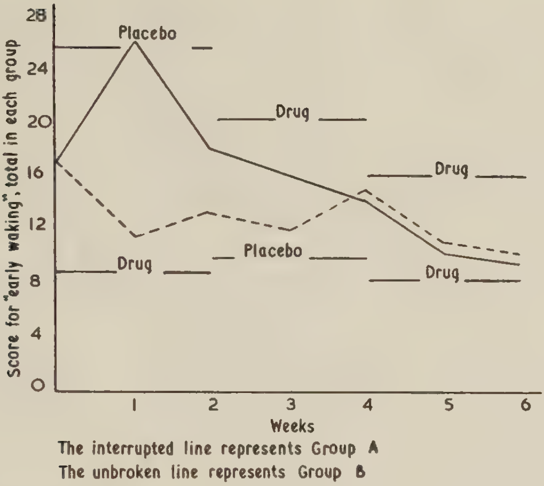


FIG. 3.—Graph showing response of "early waking" symptom to drug and placebo in the two groups.

The two groups, A and B, show a remarkable similarity in total number of symptoms (A–245, B–244), but the patients in group A showed a greater degree of depression (16 per cent.) and those in group B were much more anxious (25 per cent.).

TABLE III

Analysis of Symptoms Showing a Similar Response to Treatment in Both Groups During the First Four Weeks

	Group A		Group B	
	Drug	Placebo	Drug	Placebo
Symptom	Percentage Remission	Percentage Remission	Percentage Remission	Percentage Remission
Ideas of unworthiness ..	33·3	11·1	33·3	25
Inability to sleep ..	35	−23	21	9·5
Early waking	22·2	−14·2	21	−5·5*
Loss of appetite	11·7	26·6	0	25

* Significant at $P<0\cdot05$ (χ^2 test).

All other symptoms showed a varied response to drug and placebo in both groups of patients.

TABLE IV

Comparison of Response of Group A to the Drug and of Group B to the Placebo and Vice-versa

	Group A	Group B
	Drug	Placebo
Symptom	Percentage Remission	Percentage Remission
Inability to sleep	35	9·5*
Early waking	22·2	−5·5*
Somatic delusions	6·25	−11·5*

TABLE IV—*continued*

	Group A Placebo	Group B Drug
Agitation	−75	0*
Suicidal ideas	−16·6	37·5*
Inability to sleep	−23	21*
Early waking	−14·2	21*
Constipation	50	−11·1*
Somatic delusions	13·3	−15·6*

* Significant at $P<0{\cdot}05$ (χ^2 test).

TABLE V

Comparison of Responses During Last Four Weeks of Trial

	Group A	Group B
	Placebo: two weeks Drug: two weeks	Drug: four weeks
Symptoms	Percentage Remission	Percentage Remission
Retardation	40·1	77·4*
Ideas of reference	−20	88·8*
Inability to sleep	0	52*
Constipation	50	0*
Somatic delusions	20	0*

* Significant at $P<0{\cdot}05$ (χ^2 test).

E. *A Typical Case History:*

Miss M.F.J., age 70. She is a conscientious hard-working spinster, who had no history of depression before 1955. Then she had an attack which was characterized chiefly by financial worries and agitation. This attack responded rapidly to E.C.T. and she was discharged from hospital. In 1957 she had a second attack of depression but this one differed from the first in symptomatology. She was depressed and so grossly retarded that she had to be admitted to hospital as a certified patient. She showed marked feelings of depression, ideas of unworthiness, and her sleep and appetite were poor. Agitation and suicidal ideas were present but not prominent. She had no ideas of reference, no mood swings and no somatic delusions. She made a good initial response to E.C.T. but soon relapsed into her state of depression. Two further courses of E.C.T. were given without benefit. She remained in a state of chronic misery, being almost speechless with depression. In February, 1959 she started to take phenelzine 15 mg. t.i.d. and after two weeks' treatment she showed a remarkable degree of improvement. Her relatives were quick to note the change in her appearance, she went home on leave for several week-ends and she was finally discharged in April, 1959, after an illness which had lasted for almost two years.

DISCUSSION

At first glance there would seem to be little to choose between the response to the drug and the response to the placebo. The most important factor appears to be the initial variety of treatment. The greater response is in the first two weeks, irrespective of the form of treatment, drug or placebo. This would seem to imply that there are three possible causes of recovery: drug, placebo and spontaneous remission. There is some evidence however to show that a drug effect is present which is probably greater than the effect of either placebo or spontaneous remission. Examination of Figures 1 and 3 shows that the response to the drug is immediate and that there is a tendency for the drug effect to persist for a little while after the change to placebo. Table III shows a number of symptoms which respond similarly in both groups of patients to the drug and the placebo. These include inability to sleep and early waking, the latter showing a difference of response to drug and placebo in both groups which was statistically significant. If one compares the two groups in the manner shown in Tables IV–V, again a significant difference is demonstrated between the responses to drug and placebo for the symptoms of inability to sleep and early waking, with the exception of Table V for the symptom of early waking where the difference is not sufficiently great to be significant. It may be argued that this is not a valid comparison since the groups are not homogeneous. However they are almost similar apart from the differences in agitation and depressive ideas, described above, and one is impressed by the way in which these symptoms of sleep disturbance show a regular pattern of response to drug and placebo. They are commonly improved by the drug and made worse by the placebo. Again some psychiatrists do not accept the view that inability to sleep and early waking are characteristic depressive symptoms; but the present writers have found these symptoms constantly in these series and are impressed by the constancy of their incidence.

Although the apparent improvement after the total course of treatment is much higher for the psychological symptoms of depression, the nidus of recovery appears to be in the physiological symptoms of inability to sleep and early waking. Once these improve the psychological symptoms remit rapidly. Of interest is the response of the symptoms of loss of appetite and constipation to placebo. It is well known that in general such symptoms respond readily to placebo, but it has been thought always that the loss of appetite and constipation of depressed patients were physiological phenomena and were much more intractable to simple treatments. The treatment of depression presents a difficult problem for statistical evaluation. The illness can remit spontaneously at any time and the course of natural remission can be rapid. Once treatment has begun, the process of spontaneous remission can come into play and add its force to that of the particular treatment. In any event recovery can be swift and it is difficult to achieve a reversal of improvement either by the use of a drug or placebo after the third or fourth week of treatment. However it is felt that the results of this trial show that there is a valid response of the depressive symptoms of inability to sleep and early waking to the drug phenelzine.

At present E.C.T. is the most widely used form of treatment in depression but its disadvantages, i.e. the risk of fatal outcome (Maclay, 7) and transient memory impairment (Sargant and Slater, 8), tend to concentrate interest on a search for a simpler, safer form of treatment. Amphetamine is a drug which has been used in depression for many years, but most psychiatrists feel that it offers only temporary relief for symptoms. Indeed it tends to aggravate insomnia and loss of appetite and there is a fair risk of addiction. Iproniazid is of doubtful value since it can produce liver damage and death (Smarr, *et al.*, 9). Recently, Tofranil (imipramine) has been given a trial in the treatment of depression with some promising results (Delay *et al.*, 4) but it has exhibited some side-effects, notably skin rashes (Boyd and Forest, 2). No toxic side-effects of any description have been noted in this trial of phenelzine, but it is emphasized that no patient was given the drug for longer than four weeks. Indeed it is the writers' view that if a depressed patient is not going to respond after four weeks of any treatment there is little point in continuing with that treatment. It is apparent from Figure 1 that there is a good initial response to phenelzine and that there is an appreciable remission of symptoms after two to three weeks of treatment. Since this is the average duration of a course of E.C.T. there is a reasonable case to be made out for comparing phenelzine favourably with E.C.T. However, in the present state of knowledge E.C.T. remains the treatment of choice where the patient is so retarded and stuporose that she is likely to die from starvation.

Summary and Conclusions

A double-blind cross-over trial has been carried out on 34 female, depressed, in-patients, using a mono-amine oxidase inhibitor, phenelzine and a placebo. Nine (26 per cent.) patients have been discharged, 13 (38 per cent.) have shown great improvement and 14 (41 per cent.) have shown a slight or a moderate improvement. Five patients (14 per cent.) were made worse. The symptoms which gave a valid response to the drug over the placebo were early waking and possibly inability to sleep. Constipation and loss of appetite responded remarkably to the placebo. In view of the apparent absence of side-effects during the four weeks of the trial, the fairly rapid action of the drug and its obvious positive effect on some of the physiological aspects of depression, it is felt that phenelzine has a place in the treatment of this condition.

Acknowledgments

We wish to thank Dr. A. Walk for his helpful criticism of this paper, and Mr. F. J. Trenowden, hospital pharmacist, for supervising the details of the trial. We are grateful to Wm. R. Warner & Co. Ltd. for a generous supply of Nardil tablets.

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DEANOL IN DEPRESSION

A CONTROLLED TRIAL

By

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THE management of mild depression and its concomitant associated symptoms of general debility presents a constant and widespread challenge to psychiatry both in hospital and in general practice. It is inevitable that at some stage resort will be made to drugs. This is a tempting pharmacological field and the level of interest is indicated by the available plethora of alternatives. A recently introduced drug, in current use and purported to be of use specifically in this field is Deanol (Deaner) which is the p-acetamidobenzoic acid salt of 2-dimethylaminoethanol or Atrol which is the bitartrate of the same base.

The theoretical grounds for the introduction of D.M.A.E. (Deanol) followed observations that certain tertiary amines including arecoline, pilocarpine and eserine would inhibit certain conditioned responses in rats, and that lucid intervals in schizophrenic patients were produced by arecoline. It was concluded that the production of acetylcholine in the brain might have a beneficial stimulant effect. The agent chosen was D.M.A.E., a tertiary amine which is a precursor of acetylcholine and which can cross the blood-brain barrier (Pfeiffer *et al.*, 1957). Lemere and Lasater (1958), Moriarty and Mebane (1959) have claimed improvements from 60–70 per cent. in a series of over 150 patients finding it particularly useful in mild depression, chronic fatigue states, and nervous exhaustion. These were not controlled trials. This present paper records the result of a controlled study.

CASE MATERIAL

Twenty patients were investigated, 4 females and 16 males; 4 as in-patients and 16 as out-patients. The preponderance of male patients carries no bias of selection, simply reflecting the fact that the trial was carried out in a predominantly male unit. The average age was 37, the youngest being 26 and the oldest 57. Patients were selected for the trial if the prominent symptom was depression in the setting of an affective illness, of a degree requiring hospital treatment but not severe enough for E.C.T. Other symptoms such as fatigue, disturbance of sleep, lack of concentration, various bodily aches were not constantly present but it was the change of mood that remained prominent throughout. In 15, symptoms had been present for less than 6 months, 3 for 12 months and in the other 2 for over 3 years. For 10 patients this was their first depressive illness; in 8 their second, and, the third and fourth for each of the other 2. Seven had previously had E.C.T. One had undergone leucotomy and one had been treated with psychotherapy.

METHOD

The method used was the double-blind, self-controlled clinical trial. The basis of the trial was a comparison between the placebo and the active drug phase and not an absolute assessment. Patients received 40 milligrams of Deanol or an inert placebo. This dosage is in line with the other trials, the out-patients receiving it in one dose in the morning and the in-patients in two 20 milligram tablets morning and noon. All were informed that they were going to be treated with a new drug and the only other medication permitted was the patients' customary hypnotic at night. During the treatment only the chief pharmacist was aware of which tablets a patient was receiving at that time. It was indicated by the makers that initial improvement might be expected to occur by the end of the first week. Of the 20 patients, 5 were treated for 10 days, 10 for 2 weeks and 5 for 4 weeks on the drug and for the same period on the placebo. Patients were assessed initially at 10 days, and fortnightly. They were rated as: symptoms absent (0), slight (1), severe (2). Ideas of guilt, retardation, insomnia, loss of appetite, weight loss, and the overall state of the mood were also assessed.

RESULTS

Five patients improved, 3 during the Deanol and 2 during the placebo phase. Of these 3, 2 had been on the drug for 2 weeks and 1 for 4 weeks. The remaining 15 showed no difference in either period. These results show clearly that the therapeutic effects of Deanol were no better than those of the placebo.

DISCUSSION

The number of subjects in this trial is small but in view of the unequivocal nature of the results obtained it was felt to be unjustifiable to continue the trial further. Although these results concur with those of other workers in the absence of any side-effects, yet the significant amelioration found elsewhere in the uncontrolled trials referred to above has not been supported by this trial.

SUMMARY

Deanol, a drug reported to be useful in mild depression, was studied in a controlled trial using 20 patients. The results obtained were no better than those of the placebo.

ACKNOWLEDGMENTS

It is with pleasure I record my thanks to Dr. E. H. Hare for his help in the preparation of this paper and for permission to use patients under his care. I would also like to thank the Chief Pharmacist Mr. W. Brookes for his unfailing help.

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"NEW LAMPS FOR OLD"*

By

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FIFTY-ONE years have elapsed since the Report of the Royal Commission on the Care and Control of the Feeble-minded was published and paved the way for the Mental Deficiency Act of 1913. Since that time two developments have taken place. On the one hand the administrative procedures for dealing with defectives on the basis of the Act and its amendments have been clearly defined and formalized. On the other there has been a continuous development and expansion of our social and welfare services. These developments, which should have been complementary in their aims, have in fact often proved conflicting in effect, because mental deficiency until very recently was bound to outmoded procedures which were designed to segregate the defective from the community rather than to integrate him with it, and give him the opportunities for re-socialization which our modern welfare services afford. The original belief that a hereditary neuropathic diathesis lay at the root of most of our social ills and would sooner or later lead to national degeneracy has been replaced by scientific genetic studies, and by medical research into the aetiology of the condition, and the associated problems involved in the training and employability of the defective. Increasing professional and public recognition of the inherent faults of existing mental deficiency legislation led to the setting up of the Royal Commission on the Law Relating to Mental Illness and Mental Deficiency which published its report in May, 1957, and this in its turn has prepared the way for the Mental Health Bill which is at present in the final stages of its passage through Parliament.

The radical changes in the law relating to mental deficiency envisaged in the new Bill are a reflection of the changes that have occurred in our outlook in recent years. Fifty years ago it was believed that 80 per cent. of all mental defect was due to the operation of hereditary factors and would occur even in a favourable environment (Tredgold, 1908). So strongly was this view held in certain quarters that when the draft of the first Mental Deficiency Bill was presented to Parliament in 1912 it contained a clause which sought to prohibit the marriage of any person considered to be a mental defective. This clause provoked such strong opposition that the Government withdrew the Bill at the end of the parliamentary session, and submitted a modified Act the following year. The publication by Penrose of the results of the Colchester Survey in 1938, emphasized the importance of environmental and social factors in every case of backwardness. The challenge presented by this report to what had previously been regarded as a fundamental principle did much to arouse the interest of voluntary bodies in the problem, and has encouraged in recent years an extension of scientific research, into the causation, prevention and treatment of mental defect. In a limited number of specific conditions it has been shown that medical treatment and improved social conditions are capable of correcting many of the effects of faulty heredity.

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* Read at a meeting of the Mental Deficiency Section of the Royal Medico-Psychological Association at Lennox Castle, 17 July, 1959.

For over thirty years the view expressed by Painter (1923) that the number of chromosomes in man was forty-eight was generally accepted. The recent introduction of new techniques by various workers (Tjio and Levan, 1956; Ford and Hamerton, 1956) involving the use of hypotonic saline or citrate solutions in tissue cultures to expand the cells and separate the chromosomes, the use of colchicine to arrest chromosome division before completion, improvements in the Feulgen stain, and the use of the "squash" technique were all required before significant improvement could be obtained in mammalian chromosome counts. The first triumph for the new methods was the demonstration that man has forty-six chromosomes, not forty-eight as was formerly believed.

The second advance has been the development by Ford and his colleagues (1956) of the use of short-term cultures of sternal marrow, which has resulted in the elimination of the chromosomal anomalies which are likely to occur in tissue cultures which have been maintained for any length of time. This cumulative series of improvements has resulted in the demonstration of significant deviations from the standard chromosome complement in certain clinical conditions. The methods evolved by Ford and his team at Harwell (1958) have enabled Penrose (1959) and his colleagues to demonstrate in a mixed case of mongolism and the Klinefelter syndrome the presence of two additional chromosomes, one an acrocentric autosome, and the other a Y chromosome. This is probably the first occasion on which the presence of supernumerary chromosomes in a human cell has been demonstrated, although twenty-five years ago, Penrose (1934) postulated on an inferential basis that mongolism was due to a genetic abnormality.

Extending the work at Harwell and using the same methods Court Brown and his colleagues in Edinburgh (1959) have investigated the chromosome morphology in six cases of mongolism, and in each they have demonstrated the existence of an additional chromosome which they regard as an acrocentric autosome in the smallest size range. The implications of these findings are many, some are potentially important, and the investigation continues. In this respect it is interesting that in tuberous sclerosis, where the condition has been generally accepted as being due to the inheritance of an extra chromosome, no such abnormality has so far been found by the Edinburgh team.

The results of several social surveys have established the fact that the majority of the feeble-minded are found in families that are significantly above the average in size and with fathers who are employed in the lowest occupational grades. On the other hand the brightest children were found in families below the average in size and with parents in the professional and executive classes (Lewis, 1929; Jones, 1934; Roberts, 1935). The inverse relationship of intelligence to fertility led to the assumption that genes causing low intelligence were undergoing a progressive increase, while the complementary genes associated with high intelligence and low family size were tending to die out. In these circumstances it was considered almost inevitable that a gradual lowering of the national level of intelligence would result. The expected order of decline was estimated as being of the nature of two points of I.Q. in each generation (Burt, 1946). So far there has been no direct evidence of declining intelligence in this country. The results of two Scottish surveys of school children in similar age groups in 1932 and 1947 (Scottish Council for Research in Education, 1949), supports the view that there has been no falling off in the test performance of children in the fifteen year interval between the two surveys and there may in fact have been a slight improvement. In recent years an increase in the stature and weight of children, and a declining infantile mortality rate have been reported in many countries and have been attributed to improved nutrition and better hygiene. It has been reported by various workers that intelligence, stature and health are all positively correlated (Ashby and Stewart, 1933; Penrose, 1949) and it would appear to be a reasonable expectation that the improved social conditions which have brought about a progressive improvement in the general health of the population will eventually be reflected in an improvement in its mental health and eugenic endowment.

Whilst our views on the nature and definition of mental defect have been considerably modified in recent years, so also have our views on the best methods to be adopted in mitigating its social and economic consequences particularly with regard to the education and training of the imbecile. In Scotland at present the education of the imbecile child is undertaken at Occupation Centres administered by the Education Committees, and in England at Special Training Centres administered by the Health Authorities, as day pupils. In the past it has been customary to exclude from these centres children at the lower level of the imbecile grade where speech and body balance are poorly developed. Experience has shown however that many children formerly regarded as hopelessly retarded make a good response to training at such centres provided it is started in the early years of life. It is now generally accepted that the apparent degree of mental defect in a young imbecile gives no true indication of the degree of improvement that can result from training and as a result many children who were formerly excluded now attend and benefit from training as day pupils. In many cases training in a junior occupation centre may be continued with advantage after the defective has attained the age of sixteen years. Senior occupation centres in Scotland are at present provided and administered by the local health authorities. It would appear desirable that in order to secure greater integration and continuity of training the dual control which at present exists in Scotland should be brought to an end and that both junior and senior occupation centres should be provided by the local health authority; as has been done successfully in England for many years.

Similarly in the case of the older imbecile a series of recent studies by O'Connor and Claridge (1955) and by Gordon and others (1955) have done much to alter long established beliefs regarding their adaptability and capacity for training. These workers found that with suitable training and appropriate incentives the performance of imbeciles at commercial tasks steadily improved both in respect of speed and complexity of work undertaken over long periods of time. It has been found that under sheltered workshop conditions many are capable of earning a wage that will materially contribute to their maintenance.

With regard to high-grade mental defect a series of studies carried out by the Social Psychiatry Unit of the Medical Research Council (O'Connor and Tizard, 1954) showed that some 58 per cent. of patients in mental deficiency hospitals in London, Kent and Surrey were classified as feeble-minded. The survey showed that when the feeble-minded patients between the ages of 16 and 30 years were examined by means of a standardized series of tests they returned an average intelligence quotient of 71–74 and that there was a considerable overlap in point of test performance between the high grade defective and the dull normal. In regard to stability of behaviour the survey showed only a low incidence of gross departure from accepted standards and that while many showed milder degrees of neurotic behaviour the investigators concluded that it was better to give such individuals a chance of rehabilitation outwith a mental deficiency hospital, rather than to continue detention on the grounds of their neuroticism. These results suggest the possibility that, in the case of high grade defectives of both sexes, after a preliminary period of examination and observation in a mental deficiency hospital, many of the more intelligent would be best treated by a period of short-term rehabilitation in small hostels, or in the general community with the supervision and support of the social agencies of the Local Authority or of the voluntary associations.

It was, therefore, to a professional and public opinion conscious of the need for a closer integration of all the social services available for dealing with the problem of mental deficiency and with a more optimistic outlook regarding its effects that the Mental Health Bill, which applies only to England and Wales at present, was introduced this year. It is a courageous and enlightened attempt to bring the arrangements for dealing with all forms of mental abnormality into line with the existing arrangements for dealing with physical illness, and to secure for the mentally handicapped a general re-orientation towards community care and away from segregation in large institutions. So far as the mentally handicapped are concerned the principle of the informal admission to hospital without power of detention, compulsory detention in a limited number of cases and for limited periods of time with a right of appeal against such detention, the increased responsibility of the local authorities for community care and after-care, are all matters the need for which has long been recognized and which will receive general acceptance. In Scotland, a Mental Health Bill is at present being drafted which in its broad outline will generally conform to the English measure, but is likely to contain several important modifications if the recommendations of the Health Services Council (1959) are accepted by the Secretary of State for Scotland.

We, in Scotland, have been singularly free from the allegation of the existence of many cases of wrongful certification, wrongful detention, and lack of adequate safeguards with which the Royal Commission was confronted. This is due in no small measure to our traditional respect for the integrity of our legal system, and those responsible for its administration. We do not deal with amateurs, and have long believed that an individual should only be deprived of his liberty on the grounds of mental abnormality by a professional jurist, on account of his qualifications to assess the validity of a judicial application. In practice where compulsory detention has been considered necessary or desirable this has been effected by presenting a petition to a Sheriff for a Judicial Order. In cases where objections are raised to the granting of such an Order the Sheriff reaches a decision only after both sides have been heard. Similarly in Scotland when an Order for the continued detention of a patient in an Institution or under Guardianship is made the Board of Control have a statutory duty to inform both the patient and his relatives that such an Order has been made, and at the same time to inform both parties of their right of appeal to a Sheriff against the granting of such an Order, if they wish to do so. We believe that, not only have these measures been effective in practice, and have been administered with conspicuous fairness and impartiality; but also that they have adequately fulfilled that other important prerequisite of good legislation, that they are obviously fair and impartial in their intent and design. There are many who believe that our existing legal machinery both for the granting of Orders and for the right to appeal against them is one of the ornaments of the existing Mental Deficiency Acts and one that we are anxiously concerned to retain.

In England it is now generally accepted that the Board of Control will be abolished, and its remaining functions absorbed by the Ministry of Health. We, in Scotland, take a different view. We believe that some form of supervision of our mental hospitals will always be necessary, and that such supervision can best be given as at present by the specific appointment of medical men and women for this purpose who have had a wide experience of all forms of mental illness. We also believe that the Board of Control has a valuable function to fulfil as an authoritative and accessible tribunal for the investigation of complaints by patients or their relatives, and that in the performance of these duties it provides a strong safeguard not only for the interests of the patient but also for those responsible for their care. There is a large body of informed opinion that believes that the Board of Control has still a valuable part to play in the administration of the mental health services and that it should be retained and strengthened. It is probable that in the future the Board will be concerned mainly with patients who are detained compulsorily and that it will retain a residual right of discharge in such cases. It is also felt that it should retain the right of access to any person either in hospital or elsewhere, who they have reason to believe is unable to look after his own interests, or is improperly treated.

The radical nature of the proposed legislative changes will almost certainly create initial difficulties; but we are by nature a nation of empiricists and we shall doubtless in this situation as in the past continue to deal with specific difficulties as they arise. Legislative changes will not of themselves greatly alter the present situation; but the combination of increasing scientific knowledge and enlightened legislation does present us with an opportunity, if wisely used, to evolve a mental health service, that could prove to be one of the great social achievements of our time.

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HUNTINGTON'S CHOREA—SOME BIOCHEMICAL AND THERAPEUTIC ASPECTS*

By

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INTRODUCTION

HUNTINGTON'S Chorea presents us with a good "model" of brain disease in that we know the extent of the contribution of heredity, in contrast to a condition such as schizophrenia regarding which many authors (cf. Alanen, 1958) would be prepared to defend the concept of pseudo-heredity. Secondly the disease carries a fairly uniform prognosis, and finally it results in a distinctive disturbance of motor function which permits of some accuracy in diagnosis and some criterion for objective measurement.

One might therefore consider that Huntington's Chorea presents us, as psychiatrists, with an obvious challenge. In another hereditary condition, phenylketonuria, the error in metabolism has to a large degree been elucidated. If we cannot advance our knowledge of the aetiology of a relatively sharply-defined condition such as Huntington's Chorea then our prospects of understanding the more complex problems of the functional psychoses seem remote indeed.

Looking up the literature, one is struck by the paucity of papers reporting research into aetiology. It is true that there have been some excellent epidemiological investigations such as those of Pleydell (1954) for Northamptonshire, Brothers and Meadows (1955) for Victoria, Australia, and Reed and Chandler (1958) for Michigan. A particularly interesting paper by Reed and Palm (1951) pointed out that subjects with Huntington's tend to have larger families than their disease-free siblings, thus evading the natural tendency for diseased stocks to breed themselves out.

In the therapeutic field there was little advance until 1952 when Goldman reported on the beneficial effects of procaine amide. Goldman had noticed that one of his patients had been much improved following an injection of local anaesthetic for dental extraction.

He did not use any objective techniques of measurement, but this defect was remedied by Merskey (1958) who likewise found improvement in a proportion of his patients treated with procaine amide. Similarly positive results were reported by Ganguli (1956), whereas other authors such as Lazarte *et al.* (1955), Demyer and Dykes (1954), Pleydell (1954) and Forrest (1957) had been unable to demonstrate any striking therapeutic benefit.

Another form of treatment, the administration of dimercaprol (B.A.L.), was reported by Nielsen and Butt (1955). The analogy was with Wilson's Disease and these authors reported high values for the serum copper in two cases. However, normal serum and urinary copper levels were reported by Forrest (1957).

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* Based on a paper read at the Annual Meeting of the R.M.P.A., Glasgow, July, 1959.

In 1955 Lazarte *et al.* reported on the beneficial effects of reserpine in Huntington's Chorea, while Brodie *et al.* (1956) showed that serotonin-releasing activity is restricted to tranquillizers of the rauwolfia group. This suggested the possibility that there might be some aberration in serotonin metabolism in Huntington's. Meanwhile Armstrong and Robinson (1954) had shown that there is an aberration in indole metabolism in phenylketonuria apart from the more obvious failure in the hydroxylation of phenylalanine to tyrosine. Subsequently Pare *et al.* (1957) reported low levels of circulating serotonin and urinary 5-hydroxyindole acetic acid in subjects with phenylketonuria and suggested that impaired 5-hydroxy-tryptophan synthesis might be more closely related to mental changes than the more obvious accumulation of phenylalanine in the blood.

In 1957 one of the present authors reported the detection of what were believed to be abnormal amounts of urinary indoles from four subjects with Huntington's Chorea. The present paper reports further investigations into this problem and the results of a clinical trial comparing reserpine and trifluoperazine (Stelazine).

BIOCHEMICAL INVESTIGATION

1. *Material and Methods*

Three male subjects, diagnosed as suffering from Huntington's and fulfilling the criterion of a positive family history, were put on a standard diet. By standard we mean a diet that was the same for each patient and the same each day. The diet was high in protein and gave approximately 2,500 calories per day. It was arranged in co-operation with Mr. Godfrey, the Regional Catering Officer. Fluid intake and urine output was measured during the experimental period. As these values do not correlate with the amount of urinary indoles they will not be further considered. After the patients had been on the diet for four days the 24-hour urine samples were collected for a period of nine days. During this period the following experimental procedures were effected; intravenous administration of 25 mg. of 5-hydroxy-tryptophan on day 3; oral administration of 2 g. of dl-tryptophan on day 5; and oral administration of 1·2 g. of l-tryptophan on day 8. Aliquots from the 24-hour urine samples were subjected to chromatography.

The two-way ascending technique described by Jepson (1955) using isopropanol-ammonia and butanol-acetic acid, was employed. Whatman No. 20 paper was used and 100 microlitres of untreated urine was applied with a micrometer pipette to the point of origin. Two papers were prepared from each urine aliquot and with each batch two reference papers were run. These were prepared by applying 10 mcl. of a standard mixture to the point of origin. The standard contained 5-hydroxy-tryptophan, 5-hydroxyindole acetic acid, indole acetic acid, tryptophan and tryptamine—1 mg./ml. of each substance.

After completing the two runs and drying, the first paper was exposed to U.V.L., and then to Ehrlich's reagent. The second paper was treated with sulphanilic acid reagent. On the basis of these reactions, Rh. values and comparison with the reference papers spot identification was attempted. The spot areas were then measured using a straight arm planimeter.

2. *Results*

These are shown in Table I.

TABLE I

Daily Excretion of Indole Substances
(Area in sq. cm.)

	Day	Patient	Tryptophan	Kynurenine	Q.F.B.	X	5-H.T.	5-H.T.P.	Z	5-H.I.A.A.
	1	B	3·3		2·4					
	1	J	2·8		2·1	3·0				
	1	L	2·3			2·0				
	2	B	2·4	2·6	2·0					
	2	J	3·2	2·7	1·9	2·8				
	2	L	2·8			2·2				
25 mg. 5 H.T.P. I/V	3	B	3·0				2·0	3·2		
	3	J	2·8		2·4		1·6	3·2		
	3	L	3·3			2·4	1·6	2·9		
	4	B	2·5	5·0				2·8		
	4	J	2·8	4·8				2·7		
	4	L	3·4			1·6	1·4	2·9		
2 gm. DL-T.	5	B	3·0			2·0			2·9	
	5	J	3·2	3·5		2·2			2·8	
	5	L	3·0			2·4			2·7	2·5
	6	B	3·0			1·6			2·8	
	6	J	2·6	4·2	2·9	1·9			2·2	
	6	L	2·6			2·2			2·3	
	7	B	2·3	3·0		1·7			2·8	2·9
	7	J	3·0	2·4		1·8			2·2	3·0
	7	L	2·4			2·4			1·8	2·0
1 gm. L-T	8	B	2·9	4·2		2·6			1·6	
	8	J	3·0	5·0		2·4			1·2	
	8	L	2·0			2·0				
	9	B	2·6	3·2		1·6				1·8
	9	J	3·8	4·4	1·9	1·4				1·6
	9	L	3·2		1·6	1·6				1·8

The designations Q.F.B. and X require some explanation. The identity of Q.F.B. (quickly fading blue) is in dispute. Riegelhaupt (1958) who first gave it this name found the spot more frequently in schizophrenic urine. Rodnight and Aves (1958) consider it to be a skatole derivative, whereas G. A. Buscaino (1958) suggests that it may be a methoxy tryptamine. One of us (A.D.F.) has found Q.F.B. quite often in normal urine. Spot X is, probably, anthranilic acid on the basis of the position, blue fluorescence with U.V.L., and yellow-orange colour with Ehrlich's reagent.

The administration of 5-H.T.P. was followed by the appearance of 5-H.T. in the urine and also unchanged 5 H.T.P.

Dl-tryptophan administration resulted in the appearance of spot Z and, after an interval of 2 days, 5-H.I.A.A. Z lies at 4 o'clock to the tryptophan spot, gives a blue-purple colour with Ehrlich's, fading quite quickly to a grey colour. There were no responses to the other tests and this spot was thought to be 5 methoxy tryptophan.

The administration of l-tryptophan was followed by the expected appearance of 5-H.I.A.A.

The next table (Table II) records the spot areas of urinary indoles from two normal male controls on the same standard diet. The only experimental procedure was the administration of 1·2 g. of l-tryptophan by mouth. As can be seen from the table, that substance Q.F.B. was detected in urine from one of these controls. The ingestion of l-tryptophan was followed by the appearance of 5-H.I.A.A. in both subjects.

TABLE II

Indoles Excreted by Two Normal Subjects
(Area in sq. cm.)

	Day	Subject	Tryptophan	Q.F.B.	X	5-H.I.A.A.	Kynurenine	5-H.T.
	1	F	2·4				2·2	
		E	2·2					
	2	F	2·6				1·8	
		E						
1 g. L-T	3	F	2·5	1·2			1·6	
		E	2·8		2·0			1·4
	4	F	2·4	1·4		2·0	1·2	
		E	2·2		2·4	1·8		

Therapeutic Observations

1. *Materials and Methods*

The same three male patients as were involved in the biochemical study were included in the therapeutic trial. During the first week each patient received nicotinic acid 100 mg. t.d.s. During the next three periods, each of two weeks, the subjects received either trifluoperazine (5 mg. tablets), lactose tablets or reserpine (1 mg. tablets) three times per day. The dosage schedule was one tablet t.d.s. for two days, two tablets t.d.s. for two days and three tablets t.d.s. for ten days. The drug sequences were arranged in the usual latin square. Methods of measuring changes in the level of motor co-ordination and the degree of interference from involuntary movement, were as follows:

(a) *Peg Board Test.* This consisted of a flat wooden board containing 24 holes into which had to be fitted 24 wooden pegs. Two trials were given each morning and the time taken to complete the test was recorded with a stop-watch.

(b) *Test I* represented the time taken to tie a neck-tie. Patients with Huntington's generally have considerable difficulty with motor tasks of this sort and it was anticipated that this task might be a good index of changes in the level of involuntary movement. The task was performed pre-trial and at fortnightly intervals and the time taken was noted.

(c) *Test II* was a simple weaving task devised by the O.T. Department. Whereas both the time taken and the level of accuracy were recorded, yet in fact these values correlated quite well and for the sake of simplicity the time taken for the task was used as the index of change. This task was likewise performed pre-trial and at fortnightly intervals.

Results

The mean daily times for the peg-board test are shown in Figures 1–3.

Figure 1 shows the results in patient J. There is improvement in the test times toward the end of the first week with further improvement during the trifluoperazine (Stelazine) period. Scores deteriorate during treatment with placebo and reserpine.

Figure 2 refers to patient B. Again improvement during the first week is followed by relapse in the placebo and reserpine periods. Improvement in the test times occurs during treatment with trifluoperazine.

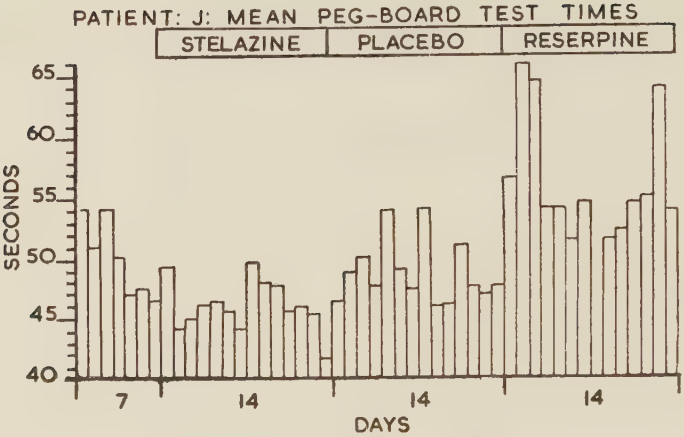

FIG. 1

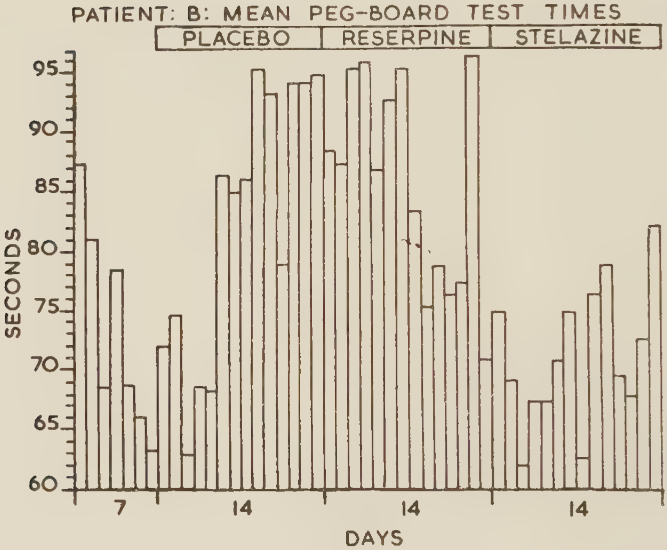

FIG. 2

Figure 3 refers to patient L. He was not very co-operative and, as you can see, on several occasions he refused to do the test at all. The test scores were recorded at the end of the first week and during the second week, while on reserpine.

The peg-board test was performed twice daily by two normal subjects for 14 days. The mean scores on the 14th day were 79 per cent. and 80 per cent. respectively of the mean scores on the first day. Applying these crude criteria to patients J. and B., it appears that their best times on trifluoperazine were 76 per cent. and 71 per cent. of their starting times. These figures are, in fact, not much different from those that might have been predicted on the basis of practice effect in the two normals.

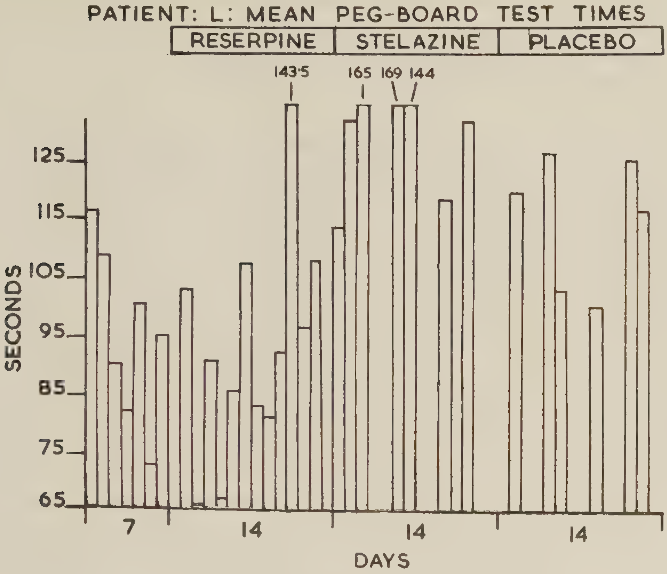

FIG. 3

However, the practice element in tests I and II were minimal and from Table III it is clear that the test scores during the trifluoperazine period were again lower than in the other two drug periods. Rather surprising perhaps are the low scores recorded during the first week when the patients were receiving nicotinic acid.

TABLE III

Results of Timed Performance Tests in Subjects J. and B. During Different Drug Treatments

Subject J.				Subject B.			
Date	Drug	Test 1 (Seconds)	Test 2 (Seconds)	Date	Drug	Test 1 (Seconds)	Test 2 (Seconds)
1/5/59 ..	—	20·4	360	1/5/59 ..	—	52	480
15/5/59 ..	S	22·4	420	15/5/59 ..	P	79	1,680
29/5/59 ..	P	30	420	29/5/59 ..	R	47·6	720
12/6/59 ..	R	67·6	540	12/6/59 ..	S	36·8	660

DISCUSSION

Previously (Forrest, 1957) one of us had reported the detection of excess indoluria in samples from patients with Huntington's Chorea. The criteria for excess were based on the paper by Jepson (1955). Subsequent experience had suggested that dietary factors were important and that a "loading test" using the amino acid tryptophan might bring out metabolic abnormalities. In fact there seemed, in this investigation, to be little difference between the choreics and the normals in their response to the ingested tryptophan. Whereas it is true that the choreics did excrete a greater total, as measured by spot area, the significance of this observation is obscure. Similar findings have been reported for schizophrenics (Leyton, 1958; Cafruny and Domino, 1958).

The results of the therapeutic trial indicated that as regards suppression of involuntary movement trifluoperazine proved more potent than reserpine.

This is not consistent with the postulate that the reserpine effect is specific and related to some disturbance of serotonin metabolism in Huntington's Chorea.

However, though we used the motor phenomena as a guide to drug effects, our object was to treat the patients rather than their movements. Subject B, in fact, showed more improvement on reserpine as judged by self-assessment and the opinion of the nursing staff. Subject J showed improvement in his mental state as well as the choreiform movements while on trifluoperazine; on reserpine he became depressed and suicidal. Subject L, who showed more intellectual deterioration than the others, made little consistent response to either of the drugs. As noted previously all three patients improved during the first week while receiving nicotinic acid. This vitamin was not used with any therapeutic intent but merely because two of the patients expected pills and would have been upset if they had been withheld. The improvement in the first week was probably a practice effect. Subsequently we treated two of the patients with large doses of oral nicotinic acid but without any striking results.

The tests we used are certainly open to criticism. We have described them loosely as performance tests and admit that completion of them largely depends on the subject's attitude and motivation. It may be, in fact, that improved times on the performance tests reflected alteration in attitude to the tests rather than any specific effect on involuntary movement. That this is clearly not the whole answer is shown by the observation that patients B and L showed increased involuntary movement at rest during the placebo period.

As regards the mode of action of chlorpromazine Bradley and Elkes (1956) have suggested, on the basis of animal experiments showing a blocking effect on arousal responses to afferent stimulation, that the drug may act in relation to the afferent collaterals entering the reticular formation at the brain stem level. As regards reserpine Gross and Weiskrantz (1959) have reported experiments on delayed auditory response in monkeys which suggested that reserpine was producing a partial "sensory blockade". We therefore treated two of our choreic patients with phencyclidine (Sernyl) on the basis that this drug induces an even greater degree of "sensory blockade". Given by the intravenous route this drug is a psychoticomimetic (Luby *et al.*, 1959) while by the oral route it has been used as a tranquillizer (Bodi *et al.*, 1959). Our two patients received 5·0 mg. t.d.s., of phencyclidine by mouth and showed quite marked reduction in the amount of involuntary movement. Unfortunately drowsiness and ataxia were conspicuous side-effects. Nevertheless these different observations suggest that there may be a common factor in the mode of action of these drugs used in Huntington's Chorea, namely a partial "sensory blockade" of incoming proprioceptive impulses.

Summary

1. An investigation into the excretion of urinary indoles and the response to a test dose of l-tryptophan in three patients with Huntington's Chorea and two normal controls is described. No specific abnormality, differentiating the patients from the normals, could be detected.

2. A trial comparing the effect of reserpine and trifluoperazine on the amount of involuntary movement in three patients with Huntington's Chorea is described. Trifluoperazine seemed, in this respect, to be the more potent drug.

ACKNOWLEDGMENTS

We would like to thank Professor A. Kennedy for access to patients; Miss C. Henderson and Miss M. Costa for arranging the performance tests in the O.T. Department, and the nursing staff for assistance in the administration of the peg-board test.

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CHLORPROMAZINE AND PECAZINE IN CHRONIC SCHIZOPHRENIA

By

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In this paper the effect of chlorpromazine* is compared with that of pecazine† on the schizophrenic population of three chronic psychiatric wards.

Delay, Deniker and Harl (1952) introduced chlorpromazine into psychiatry. Pecazine was first used by Kline and Jacob (1955) and Hiob and Hippius (1955). Thorpe and Baker (1956), in a double-blind, controlled trial, found that both drugs reduced tension significantly in deteriorated, female, schizophrenic patients. Baker and Thorpe (1957) found that pecazine did not significantly reduce daytime incontinence in deteriorated psychotic patients. The trial was controlled and blind. Jones (unpublished), in a double-blind, controlled trial on disturbed psychotic patients, found chlorpromazine to be effective but could find no evidence that pecazine had any effect.

METHOD OF PRESENT TRIAL

Three locked wards for chronic, female, psychiatric patients were chosen. They were respectively a disturbed ward, a moderately disturbed ward and a ward in which 14 of the 57 patients worked in the hospital utility departments. The patients on these wards were diagnosed systematically by the present writer. The criteria for the differential diagnosis of schizophrenia were those of Mayer-Gross, Slater and Roth (1954).

The whole schizophrenic population of these three wards was studied, excluding cases of 60 years of age and over, and also excluding cases falling within Kraepelin's category of paraphrenia systematica.

Two patients had to be dropped from the investigation at an early stage. Ninety-two patients remained, 33 in the disturbed ward, 39 in the moderately disturbed ward and 20 in the workers' ward. Following Harries (1927) the patients were assigned to three groups—A, B and C—alternately, in order of their admission to hospital. This was carried out for each ward separately.

TABLE I

	Whole Series	Group A	Group B	Group C
Age range (to nearest year)	20–59 years	20–59 years	21–57 years	24–59 years
Mean age	42·25 years	42·00 years	41·20 years	43·70 years
Time since admission to hospital (to nearest month); range	3 months– 33 years 8 months	3 months– 24 years 9 months	6 months– 33 years 8 months	6 months– 29 years 5 months
Mean	11 years 4·23 months	11 years 1·10 months	11 years 4·77 months	11 years 6·93 months

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* 2-chlor-10-(3-dimethylaminopropyl) phenothiazine hydrochloride. Largactil (May & Baker), Thorazine (Smith, Kline & French), Megaphen (German workers), Ampliactil (Spanish workers), Aminazine (Russian workers), 4560 RP, SKF 2601 A.

† 10-(1-methyl-3-piperidylmethyl) phenothiazine. Pacatal (Warner), Mepazine, Lacumin (Scandinavian workers), P 391, W 1224.

Chlorpromazine was already familiar to the nursing staff; an unfamiliar, green, 25 mg. chlorpromazine tablet was used in order to overcome this difficulty. It was sweet tasting. The 25 mg. pecazine tablets were white and slightly bitter. The placebos were white, one being sweet and the other tasteless. Neither the ward doctor nor the nursing staff knew which drug the patients were having at any time.

The patients were rated initially and subsequently every four weeks. Each patient was rated on the fifteen most valid items of the Albany Behavioural Rating Scale (Shatin and Freed, 1955), and on an additional item relating to whether or not the patient was destructive. Each item was rated 1 or 0 by the two ward sisters in charge of the daytime shifts on each ward, a score of 1 indicating variation in the direction of mental health. In each case the average of the scores awarded by the two sisters was added to the score awarded by the ward doctor on two further items—mental tension and schizophrenic thought disorder. These were also rated as 1 or 0.

TABLE II

Course of the Investigation

(The tablets of the active drugs were each 25 mg. in strength)

Week of Investigation (inclusive)	Group A	Group B	Group C
1– 4 ..	No tablets	No tablets	No tablets
5– 8 ..	Placebo 3 tablets thrice daily	Placebo 3 tablets thrice daily	Placebo 3 tablets thrice daily
9–12 ..	Pecazine 1 tablet thrice daily	Chlorpromazine 1 tablet thrice daily	Placebo 1 tablet thrice daily
13–16 ..	Pecazine 3 tablets thrice daily	Chlorpromazine 3 tablets thrice daily	Placebo 3 tablets thrice daily
17–20 ..	Chlorpromazine 1 tablet thrice daily	Pecazine 1 tablet thrice daily	Placebo 1 tablet thrice daily
21–24 ..	Chlorpromazine 3 tablets thrice daily	Pecazine 3 tablets thrice daily	Placebo 3 tablets thrice daily

Each patient's score was adjusted as a fraction of the maximum possible score (18) for each rating.

The arbitrary nature of the rating scale made statistical methods suitable for normally distributed variables inappropriate here. The numbers of patients in each group falling into high (10–18) and low (0–9·9) scoring categories were compared at various times by means of the χ^2 test.

RESULTS

One case in group A developed agranulocytosis at the end of the 15th week, and had to have placebo subsequently. She was not dropped from group A as we were attempting to assess the proportion of chronic, schizophrenic patients who might be improved by the drugs. It was not necessary to interrupt treatment in the case of any other patient.

TABLE III

In all cases, the active treatment groups showed better results than the control group C.

Week of Investigation	Groups A and C Compared		Groups B and C Compared	
0	$\chi^2=0{\cdot}03$	$P>0{\cdot}80$	$\chi^2=0{\cdot}87$	$P>0{\cdot}30$
4	$\chi^2=0{\cdot}03$	$P>0{\cdot}80$	$\chi^2=0{\cdot}87$	$P>0{\cdot}30$
8	$\chi^2=0{\cdot}17$	$P>0{\cdot}50$	$\chi^2=0{\cdot}17$	$P>0{\cdot}50$
12	$\chi^2=0{\cdot}18$	$P>0{\cdot}50$	$\chi^2=2{\cdot}83$	$P<0{\cdot}10$
16	$\chi^2=0{\cdot}84$	$P>0{\cdot}30$	$\chi^2=5{\cdot}64$	$P<0{\cdot}02$*
20	$\chi^2=5{\cdot}09$	$P<0{\cdot}05$*	$\chi^2=13{\cdot}7$	$P<0{\cdot}001$†
24	$\chi^2=3{\cdot}88$	$P<0{\cdot}05$*	$\chi^2=6{\cdot}04$	$P<0{\cdot}02$*

* indicates statistical significance beyond the 5 per cent. level.
† indicates statistical significance beyond the 1 per cent. level.

TABLE IV

Where the results have remained the same or deteriorated with time, the values of χ^2 and P are placed in parentheses. Where improvement has occurred, they are not.

Ratings Compared (given in weeks from the start)	Group A	Group B	Group C
0 and 4 ..	($\chi^2=0{\cdot}00$ $P=1$)	($\chi^2=0{\cdot}00$ $P=1$)	($\chi^2=0{\cdot}00$ $P=1$)
0 and 8 ..	$\chi^2=0{\cdot}07$ $P>0{\cdot}70$	($\chi^2=0{\cdot}00$ $P=1$)	$\chi^2=0{\cdot}00$ $P=1$
4 and 8 ..	$\chi^2=0{\cdot}07$ $P>0{\cdot}70$	($\chi^2=0{\cdot}00$ $P=1$)	$\chi^2=0{\cdot}00$ $P=1$
8 and 12 ..	($\chi^2=0{\cdot}00$ $P=1$)	$\chi^2=0{\cdot}58$ $P>0{\cdot}30$	($\chi^2=0{\cdot}00$ $P=1$)
8 and 16 ..	$\chi^2=0{\cdot}07$ $P>0{\cdot}70$	$\chi^2=2{\cdot}36$ $P<0{\cdot}20$	($\chi^2=0{\cdot}00$ $P=1$)
12 and 16 ..	$\chi^2=0{\cdot}26$ $P>0{\cdot}50$	$\chi^2=0{\cdot}28$ $P>0{\cdot}50$	$\chi^2=0{\cdot}00$ $P=1$
8 and 20 ..	$\chi^2=0{\cdot}26$ $P>0{\cdot}50$	$\chi^2=4{\cdot}27$ $P<0{\cdot}05$*	($\chi^2=0{\cdot}71$ $P>0{\cdot}30$)
12 and 20 ..	$\chi^2=0{\cdot}58$ $P>0{\cdot}30$	$\chi^2=1{\cdot}15$ $P>0{\cdot}20$	($\chi^2=0{\cdot}33$ $P>0{\cdot}50$)
8 and 24 ..	$\chi^2=0{\cdot}26$ $P>0{\cdot}50$	$\chi^2=1{\cdot}00$ $P>0{\cdot}30$	($\chi^2=0{\cdot}31$ $P>0{\cdot}50$)
16 and 24 ..	$\chi^2=0{\cdot}00$ $P=1$	($\chi^2=0{\cdot}07$ $P>0{\cdot}70$)	($\chi^2=0{\cdot}31$ $P>0{\cdot}50$)

* indicates statistical significance beyond the 5 per cent. level.

If the groups having active drugs are compared with the control group, as they are in many drug trials, the following observations may be made. During the initial four weeks on the active drugs, when the patients were having 75 mg. daily, the group which received pecazine (group A) remained no better than group C, whereas the group which received chlorpromazine (group B) improved relatively to group C. The latter difference was not significant statistically. After a further four weeks on the active drugs (225 mg. daily), the group receiving pecazine had improved, although it was not significantly better than group C. The group receiving chlorpromazine had improved further and was now significantly better than group C ($P<0{\cdot}02$).

During the last eight weeks of the investigation, when the active drugs had been changed round, groups A and B were significantly better than group C.

This method of analysis involves the danger of comparing actively treated groups with a control group which is deteriorating spuriously, as in this case. A better method is to allow each patient to act as her own control. This is permissible in chronic illness, when a fairly stable condition has been reached (Herdan, 1955). It is still desirable to retain a control group as an additional safeguard. Sharp changes unconnected with the drugs under trial may thereby be revealed.

If analysed from this point of view, group A improved slightly whilst on pecazine and chlorpromazine, but at no time did the change from the 8-week level approach significance.

Group B improved during the period when the patients received chlorpromazine, though not significantly. Significance was reached during the subsequent four weeks on pecazine ($P<0\cdot05$), although this was followed by a decline during the final four weeks on pecazine.

The three groups showed no statistically significant change in thought disorder or mental tension during the investigation.

The reliability of the rating scale was tested. The coefficient of correlation between the scores awarded initially by the two sisters on each ward varied from 0·534 to 0·628. The repeat reliability, as measured by the scores awarded by each sister initially and after four weeks, gave values of r ranging from 0·583 to 0·835.

SIDE-EFFECTS AND COMPLICATIONS

In group A, more patients gained weight whilst on pecazine than had done so during a control period of the same length (8 weeks). The difference was not significant ($\chi^2=1\cdot94$, $P>0\cdot10$).

In the case of group B, more patients gained weight whilst on chlorpromazine than during the corresponding control period. The difference was highly significant ($\chi^2=7\cdot67$, $P<0\cdot01$).

TABLE V

Side-Effects and Complications

In each case, the number of patients is given

Side-Effect or Complication	Chlorpromazine (61 patients for 8 weeks)	Pecazine (62 patients for 8 weeks)	Placebo (30 patients for 16 weeks)
Parkinsonism	0	1	0
Grand mal attacks in patients with no previous history	2	0	0
Drowsiness	2	2	0
Tachycardia	2	0	0
Orthostatic collapse	1	0	0
Dizziness	2	1	0
Thirst	0	1	0
Vomiting	0	2	1
Constipation	0	1	0
Diarrhoea	1	7	4
Haematemesis	0	1	0
Skin rash	2	1	0
Erythema solare	2	1	0
Oedema	0	2	0
Difficulty in accommodation	1	2	0
Acute glaucoma	1*	1*	0
Agranulocytosis	0	1	0
Sub-clinical jaundice	1	0	0
Pyrexia	0	0	1

* The same patient.

The only serious complication encountered was one case of agranulocytosis. This occurred in a 41-year-old woman on the 47th day of pecazine. The patient complained of a sore throat at this time. She was apyrexial. The leucocyte count was 1,350/c.mm. (neutrophils 202, Stab cells 14, eosinophils 27, lymphocytes 1,026, monocytes 81 per c.mm.). Pecazine was stopped and penicillin started. Next day a sternal puncture was performed, and the count suggested the relatively benign maturation type of agranulocytosis. Thus there were 9 per cent. of premyelocytes and 6 per cent. of myeloblasts. By the 50th day, the leucocyte count had sunk to 925/c.mm. (neutrophils 65/c.mm.). Injection of nucleotides, 10 ml. four times daily, was commenced. The blood picture improved. Injection of nucleotides was stopped on the 58th day and penicillin on the 65th day. The patient made a good recovery. She was given no further phenothiazine medication.

Discussion

The group receiving chlorpromazine improved and was significantly better than the control group after eight weeks on the drug. The group which received pecazine improved, but was not significantly better than the control group. Pecazine and chlorpromazine thereafter were seen respectively to maintain and produce results which were significantly better than those obtained with the control group. These results were similar to those of other workers (Thorpe and Baker, 1956; Jones, unpublished).

If each patient was allowed to act as her own control, the results with chlorpromazine were very much less impressive than those obtained by other workers (Vaughan, Leiberman and Cook, 1955; Thorpe and Baker, 1956; Jones, unpublished; Shepherd and Watt, 1956; Abrams, 1958).

Moreover of the 61 patients who received chlorpromazine for eight weeks, only 14 patients improved by more than 3 points on the rating scale (maximum possible score 18). Seven of these patients showed scores which were virtually as labile during the control period, and they can probably be discounted. Of the 62 patients who received pecazine only 2 patients improved by more than 3 points whilst on pecazine, if those with labile scores during the control period are eliminated. An improvement of 3 points on the rating scale represents a very meagre social gain. The time was admittedly short, but 7 patients improved by more than 3 points in a series of 61 does not suggest that chlorpromazine is a treatment of wide application in chronic schizophrenia. In this connection it is interesting to note that, at the time of writing, some three years after the investigation here described, 51 of these 61 patients are still in hospital. No less than 40 of them are on one or other of the phenothiazine drugs.

It would seem that the use of these drugs is becoming excessive in chronic psychiatric wards. They should only be continued where clear improvement has occurred. Many chronic schizophrenic patients have benefited greatly from ataractic drugs, but many others have not. These drugs appear to have replaced paraldehyde and the barbiturates as a means of allaying the anxieties of the staff.

These results give no support to the conclusions of Baker and Thorpe (1957), who stated that sweet-tasting placebos might improve deteriorated, psychotic patients by improving the personal relationships between nurses and patients. In the present trial the initial placebo tablet was sweet-tasting.

Summary

The efficacy of chlorpromazine was compared with that of pecazine. A double-blind, controlled trial was carried out on 92 female patients, the whole schizophrenic population of under sixty years of age on three chronic psychiatric wards. The patients were divided into three groups and assessed every four weeks by a modification of the Albany Behavioural Rating Scale (Shatin and Freed, 1955). After eight weeks on the drugs, the group which had had chlorpromazine was significantly better than the control group. The group which

had had pecazine was better than the control group, but not significantly so. A better method is to allow each patient to act as her own control. Analysed from this point of view, group A showed only slight improvement whilst receiving pecazine and chlorpromazine in turn. Significance was not approached. Group B showed improvement whilst on chlorpromazine, significance being approached after eight weeks on the drug. Improvement continued and significance was reached during the first four weeks on pecazine, immediately after the chlorpromazine, the group deteriorating once more during the final four weeks on pecazine. There was no significant change in the scores for mental tension or thought disorder during the investigation. The results with chlorpromazine are less impressive than those of most other workers. Only 7 out of 61 patients showed an improvement of over 3 points (out of a possible 18) whilst on chlorpromazine. It is suggested that phenothiazine derivatives are used too frequently with chronic schizophrenic patients. A case of agranulocytosis occurring with pecazine is described.

ACKNOWLEDGMENTS

I wish to thank Dr. O. W. S. Fitzgerald, Medical Superintendent at Shenley Hospital, and Dr. D. T. Bardon, Consultant Psychiatrist in charge of Female Division B, for permission to carry out this work and for their constant encouragement. I also wish to thank Ward Sisters E. Gunn, M. Harney, A. McElhill, I. Shrimpton, E. Skehan and E. Woitenik for their unfailing help. Messrs. May & Baker, Ltd., provided the green chlorpromazine tablets, and William Warner & Co., Ltd., provided the pecazine tablets and one of the placebos.

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CLINICAL TRIALS WITH MELLERIL (TP21) IN THE TREATMENT OF SCHIZOPHRENIA

A Two-Year Study

By

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THE BACKGROUND OF THE STUDY

THE authors undertook to investigate the effects of two new phenothiazine derivatives on schizophrenic patients. Over a period of two years a series of clinical trials have been carried out on approximately 260 patients, some controlled, some uncontrolled. These drugs, known as Melleril (TP21) and KS75 are chemically related. Although Melleril was ultimately selected as the drug of choice we have, for statistical reasons, included some of the findings with KS75.

CHEMISTRY AND PHARMACOLOGY

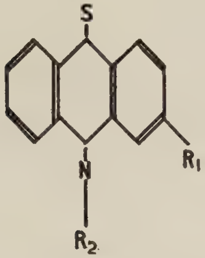
Table I shows the relationship of Melleril to other phenothiazines.

Melleril therefore differs from the known phenothiazine derivatives by the substitution of a thiomethyl group in position 2 of the phenothiazine ring. In addition, an N-methyl-piperidyl-ethyl side chain is attached to the cyclic nitrogen at position 10. It is known that substitutions in positions 2 and 10 are of particular significance for the pharmacological and clinical action of these compounds.

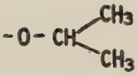
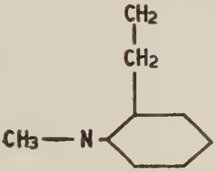
In spite of the extensive side-chain modification the drug still possesses properties basically similar to chlorpromazine, and is effective in similar doses. It seems, however, to be the side chains which are concerned with some of the side-effects of the phenothiazines. For example, if R_1 is H and R_2 is $-CH_2CH(CH_3).N(C_2H_5)_2$ we have an anti-parkinsonian agent, Ethopropazine (lydivane). Alteration of the ring structure as in Tofranil, N(γ-dimethylaminopropyl)-iminodibenzyl hydrochloride or imipramine, on the other hand, radically alters the clinical properties of the compound, and produces an anti-depressant drug.

According to Taeschler and Cerletti (1958) using mice and rats as their experimental animals it was found that Melleril reduced spontaneous motor activity in the mouse. This inhibitory effect was much more marked if the mouse had been pre-treated with amphetamine and was therefore hyperkinetic. This

TABLE I



Basic phenothiazine structure

where R_1 is:-	and R_2 is:-	Substance
$-Cl$	$-CH_2.CH_2.CH_2.N(CH_3)_2$	Chlorpromazine
 $-O-CH(CH_3)_2$		KS75
$-S-CH_3$	As KS75	Melleril

effect was greater than the inhibitory effect of Melleril on physiological hyperactivity. On the other hand, Melleril reduced hunger drive in mice significantly only when the mice were irregularly fed and were fasting moderately. In rats the conditioned flight response was not influenced by small doses (2 mg./kg.) of Melleril if the stimulus motivating this reaction persisted and reinforced the response. Without the reinforcement the inhibitory effect of the drug was in evidence with small doses.

These observations tend to show that Melleril does not elicit a general sedative effect. Amphetamine-induced excitation, hunger drive occurring outside the routine feeding time and an unnecessary flight response are more readily depressed than the more immediate response to hunger, shock and environmental adaptation. It would also be important to note that Melleril is able to inhibit an emotional reaction in the rat (emotional defecation) in doses which are well below the ones which are necessary to prevent a conditioned escape reaction, whereas the contrary is true for chlorpromazine and even more so for perphenazine.

Taeschler and Cerletti further compare their pharmacological findings with chlorpromazine and conclude that whereas the effects of Melleril and chlorpromazine on the autonomic nervous system are similar, Melleril is much less effective as a sedative and hypothermic agent and that about 10 times the dose of Melleril is required to produce the same degree of catatonia in the rat.

Less is known about the pharmacology of KS75. The limited information available to us suggests that the autonomic responses in animals are similar to Melleril.

The Design of the Clinical Trials

Reliable clinical evaluation of any new drug is notoriously difficult in psychiatric practice. Drugs which affect mental processes, such as mood and thinking, are liable to produce widely differing results in differing environments. It has sometimes been suggested that drugs such as the phenothiazines whose actions are dependent on environment cannot really be effective. These critics are referring to the difficulties experienced in measuring the clinical results.

Numerous investigations (e.g. Foulds, 1958) have drawn attention to the fact that uncontrolled trials unduly favour the apparent clinical response to the psychotropic drug being investigated. On the other hand, the inability of controlled trials to demonstrate the superiority of pharmacologically active drugs over their placebos is well known. We therefore consider that a favourable clinical impression does not by itself prove that a drug is useful any more than a statistically negative controlled trial proves that the drug is of no use. If, however, two or more investigators working as independently as possible in the same hospital, obtain a positive result with a drug both by long-term clinical use and by controlled trial, this is as far as one is ever likely to be able to go in establishing "proof" of the efficiency of the drug. This is what we have done in this trial, and we would emphasize the importance of clinical impressions with a new drug provided the investigators have already carried out several drug trials and are experienced with the use of drugs having similar pharmacological properties to the drug under trial.

We carried out four controlled trials in the wards of this mental hospital in which we endeavoured to stabilize the environment of the patients as carefully as possible. In addition to the environment, the other problem which affects psychiatric clinical trials is the method of rating or assessing mental changes during drug treatments. We designed a scale (to be reported elsewhere) which depends solely on information obtained by the doctor at the time of interview with the patient. This information can be scored as a numerical total, the higher the score the greater being the deviation from normal. This total can be broken down under eight headings—Memory, Awareness and Orientation, Perception, Sleep, Thought, Affect, Reality and Behaviour. It is a four-point scale with 53 items, some of which are mutually exclusive, the scoring range extending from 0–129. In practice scores of over 100 are very exceptional and 80 indicates a severe degree of psychiatric abnormality. Two of us (E.W. and R.A.S.) who rated the patients throughout the trial correlated well when both rated 10 schizophrenic patients ($r=0\cdot89$; when $P=0\cdot01$, $r=0\cdot76$).

The controlled trials were double blind and statistically controlled. They were carried out in various wards of the hospital, each trial being confined to one ward. Neither the nursing staff nor the authors, who rated the patients, knew whether the patients were on the drug or its placebo. The placebo tablets were of the same size, shape, colour and taste as the active tablets. Each trial lasted for twelve weeks, and the dispenser who kept the code, randomized the patients. The patients were all schizophrenics and were either chronic or subacute relapsing types. The only exception was the inclusion of two old G.P.I.s, one in each group in the trial with chronic patients. During the first week each patient was given 150 mg. of Melleril or its placebo daily in three divided doses. After the first week the dose was built up to 300 mg. daily in three divided doses and standardized at 300 mg. daily for the rest of the trial. This method, by establishing tolerance, avoided excessive drowsiness and lethargy and 300 mg.

daily appears to be the most satisfactory long-term dose in this type of patient. Patients who have recovered and are receiving long-term maintenance treatment as out-patients require less Melleril, 150 mg. daily being the optimum dose.

These controlled trials established that Melleril in the doses given resulted in a statistically significant improvement occurring in schizophrenic patient compared with the placebo. We also concluded that Melleril was therapeutically somewhat more efficacious and produced fewer side-effects than KS75. We therefore continued our clinical trials with Melleril and at this point abandoned KS75.

These subsequent trials which were uncontrolled consisted of long-term trials with Melleril in relapsing schizophrenics, lasting up to 2 years. They were designed chiefly to examine the long-term results of treatment, particularly having regard to toxicity, side-effects and dosage. This class of schizophrenic patient was selected as in all cases the response of previous attacks to other forms of treatment was known. Thus to some extent the patient was his own control.

RESULTS OF THE TRIALS

First Phase

Four double-blind trials in chronic and sub-acute schizophrenics. The results are summarized in Table II.

A further analysis of the eight different items on the rating scale showed that in trial number 3 with Melleril and placebo the scores for thought disorder were significantly improved, whilst there was no significance concerning the other fields of mental activity. This suggests that Melleril causes an important improvement in thought disorder, but does not disprove change in other types of mental activity as in some cases the possible range of scores was too small to make a t-test sufficiently sensitive.

It will be noted that the matching of the patients in the two groups which are compared is adequate. All the patients were considered to be schizophrenic and the mean scores in the two groups were very nearly equal before the trial began. All the ratings were done by two of us (E.W. and R.A.S.) but patients in any one trial series were only rated by one investigator.

Second Phase

Twenty-four patients were selected for long-term study. They were all schizophrenics and had all originally been in hospital where they had commenced treatment with Melleril. Furthermore in every case these patients had previously been treated with E.C.T., deep insulin, chlorpromazine or, in one case, leucotomy either singly or severally. Some had had reserpine and other major tranquillizers. These treatments had either failed to produce improvement or else relapse had occurred after initial improvement. All 24 patients were able to leave hospital and have succeeded in remaining out for at least 6 months whilst continuing to take Melleril. They were all invited to attend the hospital for a global assessment by two of us (J.D.C. and R.A.S.). The Powick Rating Scale was not used, as the scores would have been too low. We assessed the patients in terms of "Not improved", "Improved" and "Much improved". Generally speaking the assessment "Much improved" was only made if the patient was in full-time employment and had no appreciable symptoms. The duration of treatment with TP21 varied from

TABLE II

Results of the Four Double-Blind Trials with Melleril and KS75

Trial	Type of Patient	Drug	No. of Patients	Mean Age	Mean Duration of Illness in Years	Mean Score Before Trial on P.R.S.*	Mean Score at End of Trial	Mean Difference	Value of t Statistic	Significance
1. 26 weeks trial of KS75 and placebo	Over-active chronic deteriorated schizophrenics. Males	KS75	15	52	23	53	44	−8·8	1·2	None
		Placebo	15	47	19	53	52	−2·9		
2. 12 weeks trial of KS75 and placebo	Relapsing schizophrenics	KS75	9	35	5	36	26	−9·8	2·0	Barely significant (P=0·06)
		Placebo	7	40	5	33	34	+1·6		
3. 12 weeks trial of Melleril and placebo	Relapsing schizophrenics	Melleril	8	33	6	36	26	−10·5	2·6	Significant (P=0·02)
		Placebo	7	37	5	38	45	+4·6		
4. 12 weeks trial of Melleril and KS75	Chronic but not deteriorated schizophrenics	Melleril	16	38	6	30	20	−9·9	Zero	None
		KS75	15	44	6	27	17	−9·9		

* Powick Rating Scale

6 months to 2 years, the average being about 10 months. Twenty out of the 24 patients, 18 men and 2 women, attended and each was assessed by the 2 investigators on the same day (4 patients declined to attend). The results are tabulated in Table III. It will be noted that this is a group of patients selected for their failure to respond to treatment and that the results are very gratifying. These patients tolerated Melleril in doses of 150 mg. daily very well indeed with a commendable absence of side-effects, drowsiness being the one of which patients most frequently complained.

Discussion of the Results

Ninety-two patients took part in the controlled trials of whom 24 received Melleril. As mentioned above, 24 further patients took part in the long-term trial all of whom received Melleril. About another 150 patients received Melleril in doses varying from 100 to 500 mg. daily, but for various reasons it has not been found possible to group them in a way that can easily be presented. Much was learnt, however, from these 150 patients and the authors concluded that Melleril was superior to all other phenothiazines in its ability to bring about clinical improvement in florid and overactive schizophrenics with the minimum of side-effects.

These results may be compared with the findings of other clinicians who have reported on Melleril. Cohen (1958) treated 29 psychotic patients who required management of their hyperactivity, delusional thinking or anxiety with improvement in 62 per cent. and a commendable absence of side-effects. The dose varied from 100 to 400 mg. daily given over 3–92 days. Hollister and Macdonald (1959) reported their results in 104 psychiatric patients with a variety of illnesses, chiefly schizophrenic reactions. Of 14 patients treated in a double-blind study with successive 1-month courses of drug or placebo, 9 patients improved on the drug and only 1 on placebo. In the remainder 100–400 mg. daily produced results comparable with other potent phenothiazine tranquillizers, but only minimal side reactions were observed, chiefly drowsiness, dizziness and nasal stuffiness. In doses of 2,000 mg. extra-pyramidal effects, seizures and excitement did not occur. Fleeson *et al.* (1958) conducted a placebo trial with 60 out-patients using Melleril and KS75. Twenty-three of these patients suffered from psychoneuroses, 30 from psychosis and the remainder were classed as "sociopathic reactions". Twelve out of 15 patients treated with Melleril were improved, a result significantly better than that obtained with KS75 or with the placebo. Kinross-Wright (1958) reported on the use of Melleril in 198 institutionalized and ambulatory patients in a wide range of disorders ranging from severe psychotic disturbances to minor nervous and functional disorders. The drug was well tolerated in doses of 75 mg. to 2,400 mg. daily. Side-effects were notably absent, and it was noted that some patients forced to interrupt treatment with other phenothiazines because of extra-pyramidal symptoms were able to continue therapy with Melleril without the appearance of parkinsonism. The results were best in the acute psychotics, but chronic psychotics and neurotics also derived considerable benefit.

Effects of Melleril in Psychosis

Our work to date suggests that acute and subacute schizophrenia, particularly of the paranoid and floridly symptomatic type, responds best to Melleril. In many cases, however, long-standing cases have improved and in all cases of schizophrenia except those which are completely apathetic and burnt out

TABLE III

Follow-up of Long Term Patients Who were Discharged on TP21

Case No.	Sex	Age	Diagnosis	Response to TP21 Assessed by R.A.S.	Response to TP21 Assessed by J.D.C.	Duration of Treatment with TP21
1	F	27	Hebephrenia	Improved	Improved	2 years
2	M	24	Schizophrenia	Much improved	Improved	7 months
3	M	38	Schizophrenia	Much improved	Much improved	1 year
4	M	28	Schizophrenia	Much improved	Much improved	11 months
5	M	27	Schizophrenia	Improved	Improved	7 months
6	M	29	Schizophrenia	Much improved	Much improved	1 year 10 months
7	M	36	Paranoid schizophrenia	Improved	Improved	10 months
8	M	37	Paranoid schizophrenia	Much improved	Much improved	10 months
9	M	27	Schizophrenia	Much improved	Much improved	10 months
10	M	33	Schizophrenia	Much improved	Much improved	6 months
11	F	28	Relapsing schizophrenia	No change	No change	11 months
12	M	32	Schizophrenia	Improved	Improved	10 months
13	M	26	Schizophrenia	Much improved	Much improved	1 year 2 months
14	M	16	Schizophrenia	Much improved	Much improved	7 months
15	M	36	Paranoid schizophrenia	Improved	Improved	1 year 3 months
16	M	32	Paranoid schizophrenia	Much improved	Much improved	1 year 4 months
17	M	32	Paranoid schizophrenia	Much improved	Much improved	11 months
18	M	22	Schizophrenia	Improved	Much improved	9 months
19	M	27	Paranoid schizophrenia	Much improved	Much improved	6 months
20	M	38	Schizophrenia	Improved	Improved	7 months

some improvement can be expected. This is particularly true in the case of paranoid schizophrenia and paraphrenia, and a number of long-standing cases are now living at home and leading a useful social life free of symptoms whilst continuing to take Melleril. Depression does not respond and may be made worse. The manic phase of manic depressive psychosis can be controlled but the subsequent depressive phase is not prevented despite continued treatment. Puerperal psychosis responds provided depressive features are absent. Melleril has a place in the geriatric field and of 9 elderly confused and overactive patients who received Melleril, 6 received benefit. In the chronic wards of the hospital Melleril is highly successful in controlling anti-social and aggressive behaviour without any great incidence of side-effects.

SIDE-EFFECTS OF MELLERIL

The side-effects which we have observed during trials with Melleril have not been of a serious nature and we believe that the claim can justly be made that Melleril has fewer side-effects than any other of the phenothiazine compounds.

Generally speaking the side-effects of the phenothiazines can be grouped under 5 headings:

1. Those associated with the anti-cholinergic effects of the drug.
2. Parkinsonism and extra-pyramidal symptoms.
3. Allergic responses and water retention phenomena.
4. Disturbances of liver function.
5. Disturbances of autonomic function probably the result of pituitary depression.

These are the common ones. Others such as granulocytopenia and retinal changes have been reported.

As a result of two years' experience with some 200 patients we are satisfied that the only side-effects worth mentioning are those associated with the anti-cholinergic properties of Melleril and its effects on the brain stem and pituitary function. We have not seen any cases of depression of liver function and no cases of jaundice have occurred and so far no allergic reactions or water retention has been noticed. In fact we have treated at least one patient who manifested severe allergic reactions with other phenothiazine compounds but tolerated Melleril perfectly satisfactorily. One does not, therefore, anticipate any difficulty resulting from skin rashes or oedema of the tissues.

Amongst the most common side-effects which we have noticed was drowsiness. This depends on the dose given. A few patients complained of it who received 150 mg. daily. Most patients will complain of drowsiness on 300 mg. daily although we have had an occasional patient receiving 400–500 mg. daily who did not complain of this symptom and these were usually patients who were rather severely disturbed mentally. A few patients on long-term treatment who had left hospital gave up taking the tablets on account of drowsiness, although these symptoms can be controlled by dexedrine to some extent. This also has the advantage that it tends to counteract the tendency to gain weight.

Dizziness and faintness due to hypotension sometimes occurred at the beginning of treatment and can usually be avoided by stepping up the dose at weekly intervals. It is not a serious complication.

Next in order of importance was amenorrhoea in the women and perhaps less commonly inadequacy of sexual function in the men. In some groups of patients of child-bearing age the amenorrhoea occurred in up to 50 per cent. of cases, but as these were all schizophrenics it may be partly attributed to the illness itself. Patients in the group receiving long-term treatment tended to menstruate again after about six months although somewhat irregularly. It did not seem to us to be of any clinical importance although some of the patients became anxious about it. In all cases menstrual function returned after we stopped the tablets. In 2 patients lactation occurred and this ceased after diminishing the dose of the tablets.

Other side-effects occasionally complained of were nasal stuffiness and dryness of the mouth. There were, of course, other complaints of disturbances of bodily function but we felt that these were not due to the tablets themselves. No patient complained of visual disturbance and tests showed no changes in the visual fields or of retinal function.

Parkinsonism is a rare symptom. This may be because few of our patients received more than 300 mg. daily although in our opinion it is not necessary to exceed this dose in most cases. It only occurred to any extent in 3 patients, 2 of whom were brothers and who deteriorated mentally as the parkinsonism progressed. This is worthy of comment, as in the past workers with other phenothiazines have felt that treatment is more efficient when parkinsonism is allowed to develop. Four patients who developed disabling parkinsonism on chlorpromazine had none on similar or higher doses of Melleril and at the same time improved mentally.

Dosage

This has already been discussed but will now be summarized. A parenteral form of Melleril is not yet available and all doses refer to oral administration of tablets. In psychosis 150 mg. daily in three doses is a useful commencing dose but in acute cases an initial loading dose of 200 mg. can be given followed by 100 mg. 4 or 6 hourly until control is obtained. In less severe cases the dose may be increased during the second week to 300 mg. daily and in more severe cases may be reduced to this level after a few days. Maintenance doses vary from 75 mg. to 300 mg. daily but 150 mg. daily is the average. It is important to reduce the dose as the patient improves. Psychotics of some duration needing long-term maintenance treatment who have been discharged from hospital require observation and should be seen at first at weekly intervals, extending the time to 4-weekly intervals after 2 or 3 months. In neurotic tension states somewhat lower doses may suffice.

Summary

Melleril or thioridazine is one of a new series of phenothiazine derivatives which is effective in schizophrenia and is believed by the authors to be the most effective high-dose phenothiazine available for the management of the psychoses.

Melleril has been given to 200 psychiatric patients over a period of 2 years. During this period it has proved itself to be safe and to be singularly free from side-effects, particularly extra-pyramidal and allergic complications. Controlled double-blind trials have demonstrated it to be superior to placebo tablets and to its close rival, KS75.

Melleril is most effective in the treatment of acute and subacute schizophrenia and in the management of long-standing paranoid schizophrenia and

paraphrenia. Many of these patients have been able to leave hospital and are leading normal and productive lives on long-term maintenance treatment.

The dose required varies from 300 mg. to 500 mg. daily in the acute case to an average of 150 mg. daily for maintenance treatment.

ACKNOWLEDGMENTS

We should like to thank Dr. K. W. Cross, Department of Medical Statistics, University of Birmingham, who kindly carried out the statistical analysis for us.

We should also like to thank Dr. A. M. Spencer, Medical Superintendent, Powick Hospital for his active interest.

Sandoz Products Ltd., have generously supplied the Melleril and KS75 and our thanks are due to their research department for assistance.

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EFFECTS OF REPETITION OF VERBAL SIGNALS UPON THE BEHAVIOUR OF CHRONIC PSYCHONEUROTIC PATIENTS*

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STUDIES of the effects of the repetition of statements, i.e., verbal signals, upon the behaviour of chronic psychoneurotic patients have been carried out in the Allan Memorial Institute continuously since 1953 (1).

The verbal signals used in our earlier studies were taken directly from communications made by patients in psychotherapy. Repetition was limited to 10–20 minutes. The patient was not specifically prepared. We found that this procedure evoked considerable activation of the topic from which the statement was taken. The patient would return repeatedly over the next several weeks to ruminate over the topic and this, in turn, brought back into his awareness a considerable number of related memories which he had long forgotten. As a consequence, there was a general activation of the topic and, usually, the emergence of a new pattern of behaviour relative to the matter concerned.

These early studies established the central fact upon which our subsequent investigations have been based, namely, that the exposure of the individual to the repetition of verbal signals will produce a change in behaviour and that the nature of the change will bear a relation to the content of the signals.

For instance, signals drawn from a psychotherapeutic passage concerning the patient's difficulties with his father might produce an activation of the whole topic of his relationship to authoritative figures, with a subsequent increase in confidence and decrease in hostility in such situations.

Our work since then has been directed to the discovery of means (*a*) whereby we could gain precision in predetermining the nature of changes brought about by repetition and (*b*) whereby the duration of these changes could be prolonged.

Two years ago we reported that it was possible regularly to produce predetermined changes in the behaviour of chronic psychoneurotic patients by exposing them to repetition, and that in a proportion of such cases these changes had become lastingly incorporated in their behavioural patterns (2).

We are now reporting the most recent advances which we have been able to make:

Relatively early, we found that progress could be facilitated by breaking up our problem into component parts for separate study. These are:

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* Read by D. Ewen Cameron at the Annual Meeting of the Royal Medico-Psychological Association, Glasgow, July 1959

I. The Preparation of the Verbal Signals

In order to produce the specific changes which we planned, we found that we could not depend on the chance that satisfactory passages would appear during psychotherapeutic exchanges. Hence, we explored the possibility of constructing verbal signals directly. We found that this was successful, and we now prepare our signals from material derived from psychiatric and from psychopharmacological interviews, from social service reports and from psychological tests.

In a word, when we attempt to replace an undesirable personality characteristic, we construct our verbal signals from those facts concerning its origin and maintenance, as well as from data about the desires and attempts of the patient, and those of the meaningful figures around him, to change that characteristic.

The signals are set up in two forms—a procedure termed "reversed driving". The first—or negative—form consists in those criticisms of the characteristic which have been made over extended periods of time by or to the patient. The second—or positive—form consists in those aspirations which the patient has expressed with regard to changing the undesired characteristic.

The structure of our signals falls into four parts:

(*a*) Problem identification—this is essentially what we have described as the negative phase. This serves to bring sharply before the patient the problem as it exists in terms of his own criticisms and in terms of the criticisms of those with whom he lives and works.

(*b*) The second component is the setting up of a goal. This goal may be either the changing of an undesirable attitude (e.g. a feeling of inadequacy), an undesirable relationship (e.g. excessive dependency), or an undesirable mechanism (e.g. habitual repression of hostility).

(*c*) The third component is the inclusion of a mechanism whereby this goal may be achieved; such mechanisms being selected on the basis of those commonly observed in the course of psychotherapy, such as expanded use of "talking out" with others, or the progressive expression of resentment—first in minor situations and then in critical situations.

(*d*) Lastly, we include statements aimed at giving motivation in the form of social acceptance, anticipation of greater freedom and anxiety reduction.

The following are examples of the signals used:

Negative signal—"Madeleine, you let your mother and father treat you as a child all through your single life. You let your mother check you up sexually after every date you had with a boy. You hadn't enough determination to tell her to stop it. You never stood up for yourself against your mother or father but would run away from trouble rather than make a stand. They used to call you 'crying Madeleine'. Now that you have two children, you don't seem to be able to manage them and keep a good relationship with your husband. You are drifting apart. You don't go out together. You have not been able to keep him interested in you sexually."

Positive statement—"You mean to get well. To do this you must let your feelings come out. It is all right to express your anger, we all do, and people will understand and go on liking you just the same. Let your feelings out and you will feel more confident. You want to stop your mother bossing you around. Begin to assert yourself first in little things and soon you will be able to meet her on an equal basis. You will then be free to be a wife and mother just like other women."

II. Preparation of the Patient

The second component into which we have broken down these investigations is the preparation of the patient. When we first began to explore the field of prolonged exposure to repetition, it was found that the individual, after undergoing repetition for quite brief periods, experiences increasing discomfort and seeks to move out of the area of exposure. In order to keep the patient under the particularly long periods (20–30 days, 16 hours a day) found requisite to achieve maximal incorporation of our signals, it was necessary to develop specific means. These means had to ensure that he stayed in the area of repetition whilst he remained maximally receptive.

The most effective procedure thus far developed is to keep the patient under a combination of sernyl and largactil. The first—1-(1-Phenylcyclohexyl) piperidine monohydrochloride—blocks extraneous sensory input in degrees varying with the dose and produces underactivity because of its effects on the motor system. Largactil potentiates the effect and controls whatever anxiety may be attendant upon the use of sernyl. In successful cases, a passive receptive state with a heightened awareness of the verbal signals is obtained. In certain chronic psychoneurotics where neurotic mechanisms appear particularly structured, these are broken up by means of intensive electroshock before starting repetition.

III. Delivery of Verbal Signals

The third component of our problem is the delivery of the verbal signals (see illustration). This is carried out by means of a continuously run magnetic tape. The negative phase is carried on until the patient shows growing rejection of the statements. This usually takes about 10 days; the tape running from 6 a.m. to 9 p.m. A pillow speaker is used. The positive phase is ordinarily carried on for another period of 10 days. In order to evoke maximal attention by the patient, the signals are varied in intensity; the period between the signals is also varied from a few seconds to as long as ½ hour. Moreover, signals are interrupted at crucial points in their presentation to increase the anticipation of the patient.

Finally, we have attempted to intensify the effect of the negative phase by applying galvanic stimulation to the leg; this being synchronized with the end of each negative repetition.

IV. Reinforcement

The fourth component is reinforcement. Experience early showed that better results were obtained where the newly-established pattern of behaviour was reinforced by acceptance of it and encouragement from the staff and, particularly, by acceptance and encouragement from relatives, who are especially briefed on this point.

V. Assessment

The fifth component is assessment. This is difficult. It should be recognized at the outset that there is a difference between removal of the psychoneurotic

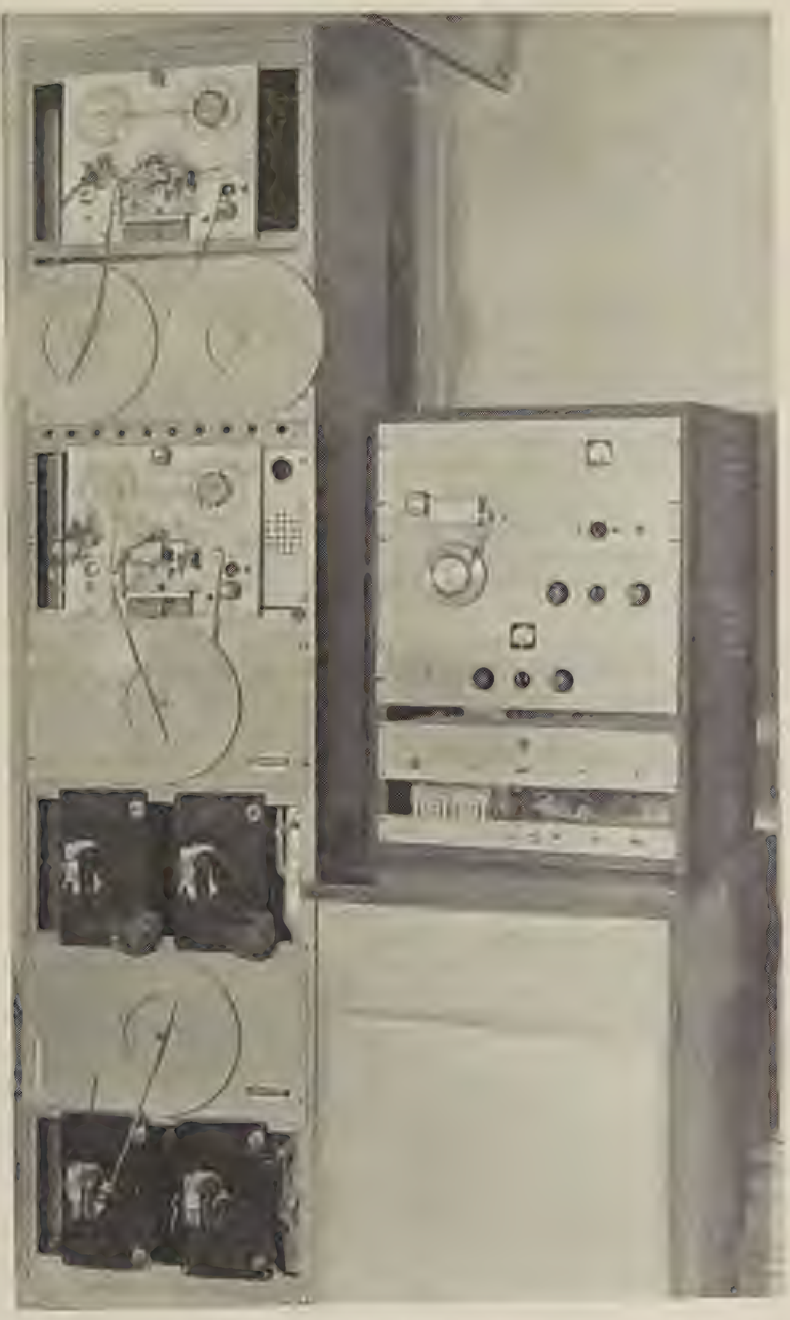


FIG. 1
A special mechanism has been built at the Allan Memorial Institute which enables us to co-ordinate delivery of eight separate sets of signals simultaneously.

symptoms and our objective, namely, change in personality traits, and yet the two undoubtedly are related. It would, for instance, be hard to imagine that a personality trait of passivity could be changed without at the same time modifying the psychoneurotic symptoms which were based on this characteristic. Indeed, in many respects, it is reasonable to say that the achievement of changes in the personality characteristics of a psychoneurotic patient constitutes an extension of the elimination of symptoms.

With regard to the actual methods of assessment, we have found that psychological tests (which include the Rorschach, T.A.T., figure drawings and Carl Rogers' Q-sort tests) are less successful than clinical assessment. Some of the tests are too susceptible to day-to-day changes. Others continue to reveal traits which, while presumably still present, are no longer active. Integration of reports from the relatives and staff has provided a considerably more reliable guide to progress.

During the period of exposure to repetition, the patients were questioned every two hours by nurses as to their ability to repeat the verbal signals and their reaction to them. This serves both to keep in touch with the change produced by the signals and to reinforce the attention given by the patient to such signals.

We have attempted to differentiate between the effects of the agents which we have used to immobilize the patient, i.e. sernyl and largactil and electroshock, which we use on rare occasions to break up particularly structured neurotic mechanisms, on the one hand, and exposure to repetition on the other. This we have done in two ways: first, we have explored the effects of this procedure in changing physiological functions. Together with Dr. R. B. Malmo, we carried out a study on the possibility of shifting the degree of emotional tension from the group of muscles in the forearm which were predominantly tense to those which were less tense (3). We did this by putting the patient through the above-described procedure; the signals used being "Your right arm is straightening out. Your right arm feels as if you are reaching out for something. Your right arm feels stiff at the elbow as it does when you are stretching." The results of all four cases on which we experimented were positive, and an illustration (Fig. 2) is provided under the title "Change from Flexor Dominance to Extensor Dominance Associated with Driving".

A second line of attack on this problem has been the inclusion of tracer statements in the verbal signals. These are statements which have nothing to do with the nature of the psychoneurotic illness or the personality of the patient. For instance, we have included a statement in the positive signals that the patient will want to touch others while talking to them. In the two cases in which we have done this, this tendency appeared for a week or two in one case and, in the other, it appears to have become lastingly incorporated in the behaviour of that individual. It is clear that these two findings could not be brought about by any agent other than repetition of verbal signals.

PROCEDURE

In our most recent series, we have employed a procedure which incorporated all the advances to which reference is made above. We carried out this procedure in a series of ten psychoneurotic patients (see Table I).

In brief, they were exposed to 10 days of repetition of negative phase signals and 10 days of positive phase signals and kept in a semi-sleep state by

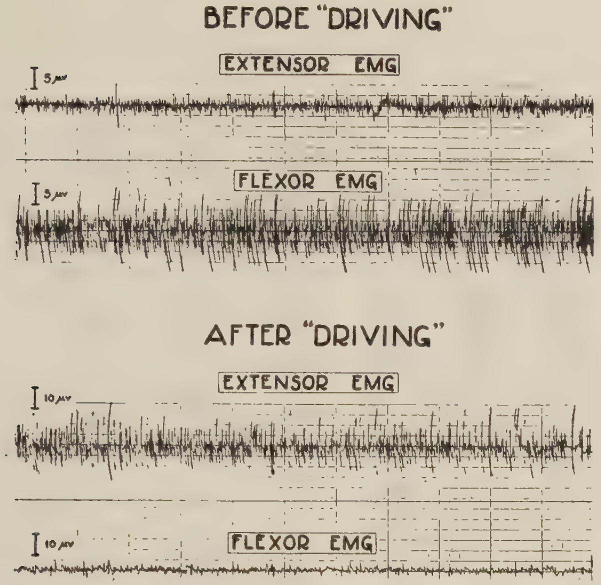


FIG. 2—Change from Flexor Dominance to Extensor Dominance Associated with "Driving".

TABLE I

Case Material

Case No.	Age	Sex	Duration of Illness	Diagnosis	Prior Treatment
1	36	F	14 years	Anxiety neurosis	Tranquillizers, psychotherapy
2	24	F	3 years	Anxiety hysteria	Tranquillizers, psychotherapy
3	32	F	13 years	Mixed psychoneurosis	Insulin, tranquillizers, psychotherapy
4	27	M	2 years	Character disorder	Tranquillizers, psychotherapy
5	52	F	5 years	Character neurosis	E.C.T., tranquillizers, psychotherapy
6	37	F	31 years	Character neurosis	Tranquillizers, psychotherapy
7	38	F	29 years	Chronic anxiety state	Tranquillizers
8	26	M	12 years	Inadequate personality	Tranquillizers
9	28	F	3 years	Character neurosis	Insulin, tranquillizers, psychotherapy
10	21	F	4 years	Anxiety hysteria	E.C.T., tranquillizers, psychotherapy

a combination of sernyl and largactil with occasional barbiturates. In four patients, electroshock therapy was used in addition to break up particularly resistant psychoneurotic mechanisms. Reinforcement was carried out throughout and the patients were assessed, as described, before and after exposure to repetition.

RESULTS

As indicated earlier, assessment has been a matter of singular difficulty. Hence we have attempted to provide several different forms of assessment. All clinical assessments represent the average of repeated evaluations by three psychiatrists and two research nurses.

Table II shows the changes in symptoms and personality traits subsequent to exposure. The degree of such change in symptoms and traits is based upon reports received from the staff, including the three psychiatrists mentioned above and a group of especially trained nurses. The degree of change was also based upon the reports of relatives and, finally, upon the report of the patient.

TABLE II*a*

Changes Produced in Symptoms and Personality Traits by Exposure to Repetition.

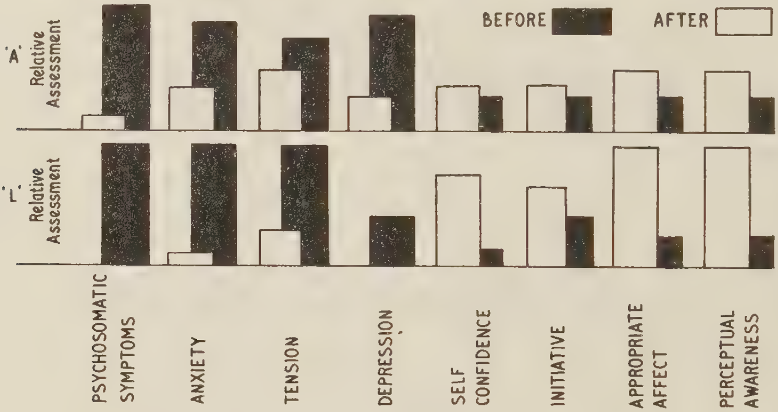


TABLE II*b*

Changes Produced in Symptoms and Personality Traits by Exposure to Repetition.

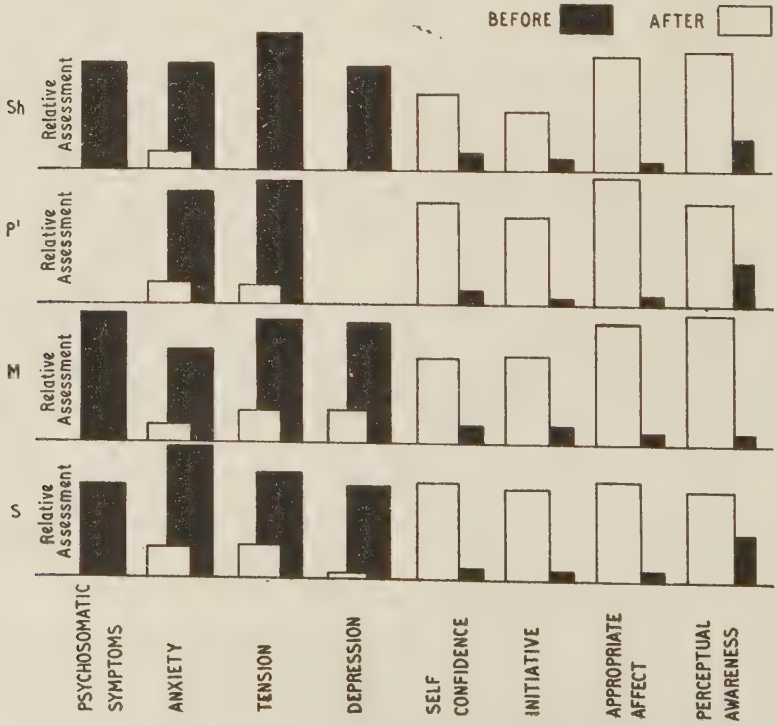


TABLE II*c*

Changes Produced in Symptoms and Personality Traits by Exposure to Repetition.

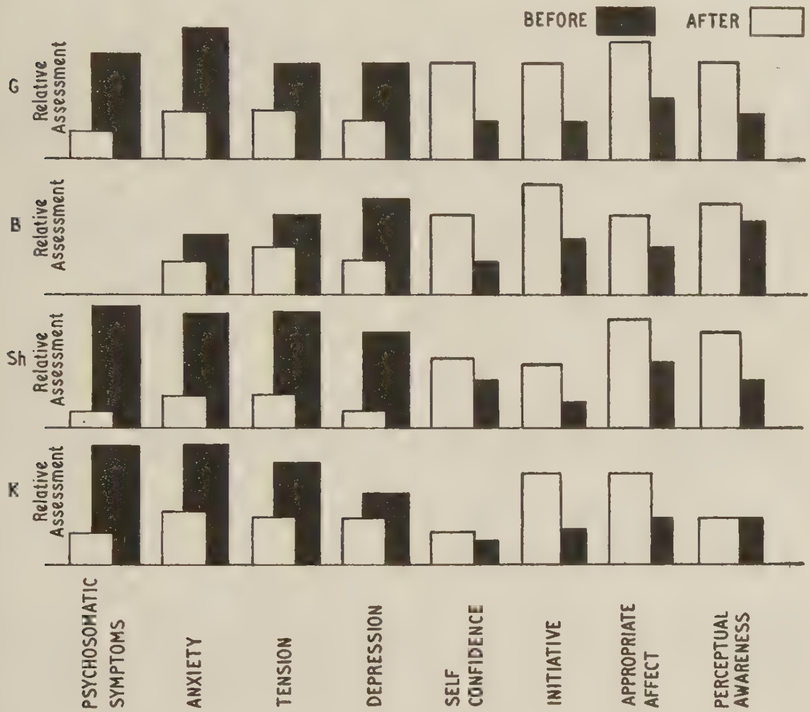


Table III presents in similar graphic form the changes produced in personality functioning as estimated by the psychologist.

TABLE III

Favourable Changes Due to the Direct Pick-up of Verbal Signals.

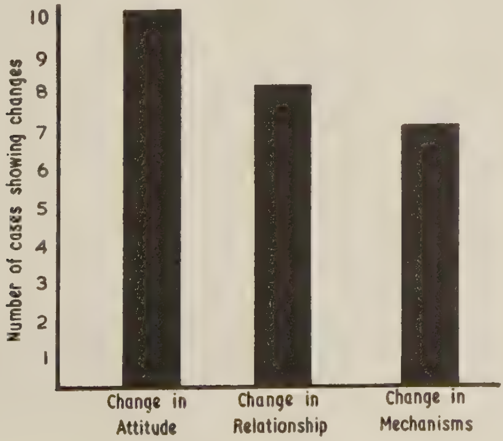


Table IV presents a report of changes in verbal form from the staff, relatives and patients.

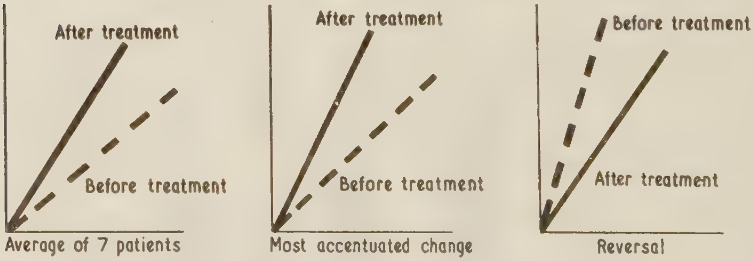
TABLE IV

Case No.	Characteristic Descriptive Statements Assembled from Patients, Relatives and Staff
1	Patient states he feels "changed and rejuvenated", "a different person".
2	Patient states that she is more relaxed, she feels much more comfortable and she does not worry about things like she used to.
3	Relatives report a marked change—patient being more responsible and capable.
4	Patient feels completely changed; says, "Things look different" . . . "I can enjoy things more" . . . "I see things more clearly" . . . "I get along with people better. I feel more confident."
5	Patient feels much more independent, sees herself separate from her mother, less concerned about other people's opinions.
6	Patient feels different, less concerned about mother's dominance, clearer in her role as wife and mother.
7	Relatives state, "She is a changed person, more interested in things and people, much more confident. She gets along with people better."
8	Patient says she no longer feels tense and anxious. She sees her relationship with people differently, feels more confident and is able to express herself more readily.
9	Patient feels more confident, less anxious, happier and more independent.
10	Patient states he feels that he is able to see his problems more clearly, is more confident and assertive—less fearful of people.

Furthermore, we have attempted to assess the degree of change by examining movies taken before and after exposure to verbal signals. The analysis of these movies is as yet too elementary to allow us to detect with any penetration the degree to which specific parts of signals are taken up. It does permit us to demonstrate change. These changes are with respect to psychomotor behaviour—greater freedom of movement, return of associated and accessory movements, and an interesting change in the degree of flexion employed in getting up from a chair. This latter change is shown on *Table V*.

TABLE V

Trunk Axis Angle of Patients Sitting Down.



It should be stressed that the process of incorporation of the signals is not a passive and mechanical one of printing in the new pattern. The patient participates actively as is shown both by the continuous ruminations recorded in the 2-hourly checks made by the nurses during the period of exposure and also by the form in which the signals become ultimately incorporated into the on-going behaviour of the patient. This active participation is in accordance with the learning theory.

The process of active participation is exemplified by a patient examined three months after exposure. At that time she said that during the time of her exposure, the negative signals seemed to her to be criticisms made in the voice of her domineering mother. Of crucial interest is the fact that she had translated part of the positive signals into a form particularly well suited to the needs and attitudes of a girl brought up in an authoritative Catholic home. The positive driving statement was "You are looking forward to going out and being happy as a wife and mother. You have gained a lot of confidence and the old problems of the past are disappearing." This she had rearranged in her own mind so that now, three months later, she says she recalls the voice as being that of one of the investigators, saying that she must remember that her family is just her husband and her two children, and her house, that is all. This served to delimit her area of responsibility and, hence to reduce her anxiety.

Discussion

The value of the procedures which have been presented is twofold: First, they provide a tool whereby direct, controlled changes in personality may be made. Obviously, what has been achieved with respect to psychoneurotic patients can be extended to any field in which there is malfunction of the personality whether within the area of psychiatry or not. Secondly, important theoretic vistas are opened up. It is clearly demonstrated that reorganization of the personality may be brought about without the necessity of solving of conflicts or abreaction, or the reliving of past experiences. While these long-held therapeutic concepts have been useful, and continue to be, there is evidence that they have begun to reach their limits and, indeed, in recent years have shown only too plainly that they are beginning to act as a straitjacket to creative thinking.

We consider that reorganization of the personality can be achieved in several ways and that what our procedure brings about is a direct building of new personality traits; the older, undesired characteristics remain but are put out of circuit.

Another matter of theoretical importance is the demonstration of repetition as a powerful force. The human organism universally seeks to escape from repetition save where its effects are desired.

Our working premise is that for organisms—particularly human organisms which are so intensely adaptive—the constantly recurring impact of an imperative to change, such as is contained within the verbal signals, constitutes a mounting pressure which the existing organization of the personality resists, but to which it continually yields in greater or lesser measure.

The validity of this premise is supported by the very considerable number of mechanisms which the human subject possesses and which serve to protect him against the impact of repetition. In an earlier publication (4), we have described those which can be seen at the behavioural level: the patient may listen without paying attention; he may react to block the effects of the signal by denying their truth or he may protect himself by misinterpreting the content of the signals.

At the neurophysiological level, a number of mechanisms are also actively engaged in blocking the effects of repetition. Sharpless and Jasper (5), who have studied habituation of the arousal reaction, have listed as additional mechanisms which bring about decrement of response to repetition of stimuli, the following: sensory adaptation, nerve accommodation, effector fatigue, Pieron's association fatigue (6), and Pavlov's internal inhibition (7).

R. Hernández-Peón *et al.* (8) have described how afferent impulses may be blocked by a shift in attention. There is growing evidence that inhibition may actually take place at the peripheral sensory organs.

It is because of this intricate series of mechanisms which act to protect the organism against the impact of repetition and, hence, to preserve the existing personality organization, that we have found it necessary to use extremely long periods of exposure to repetition, continually to re-direct the attention of the patient to the signals and to use electroshock where the undesired personality structure is particularly fixed.

Turning from theoretical considerations to practical results, we may say that, while the effectiveness of our techniques has gradually increased to the point where exposure to repetition will produce predetermined change in all cases, we wish clearly to state that these changes remain limited in the following respects: (*a*) kind, (*b*) durability.

With regard to the kind of change, we have found that the best results can be obtained if we attempt to change a characteristic which has already been recognized by the patient as deviant and undesirable. Our working premise is that where such a characteristic has already been identified by the patient, where he has wished to change it, he has already made many attempts both in reality and in fantasy to do so and to substitute a desirable trait.

In a word, what might be termed a "contra-trait" is already in existence, but is prevented from coming into operation because of the well-recognized tendency of on-going traits to persist. When considering the total personality, this persistence of the on-going personality structure has been designated by various authors as psychobiological homeostasis. When considering neurotic traits, it has been designated by other writers as the repetitiveness of neurotic mechanisms and their imperviousness to modification even where they are entirely unrewarding.

We have been able to identify certain of the mechanisms which operate at the symbolic level to maintain the on-going pattern of behaviour despite the pressure to change exercised by the continuous repetition of verbal signals, and these have been listed earlier as denial, misinterpretation, and simply not listening. We have subsumed these and other mechanisms which we suspect to be present, but cannot yet designate, under the general term of "the switcher". The term expresses the fact that the mechanisms operate so as to switch the incoming verbal signal away so that they do not reach a point where they can produce the desired changes.

In our view, repetition results not in the destruction of the undesired trait but in its loss of dominance—the formerly dominant undesired trait being replaced by the hitherto inactivated contra-trait. We should like to emphasize that the undesired trait can, and in unsuccessful cases does, regain its dominance.

Theoretically, we consider it probable that contra-traits underlie all dominant traits. However, where the patient does not recognize his deviant trait as such, then, clearly, contra-traits—if they exist at all—have not been acted out by the patient in reality or in fantasy. Thus, they are more feebly organized and less capable of being substituted for the dominant deviant traits through our procedures.

The validity of the concept of the contra-trait is strengthened by the fact reported earlier in the section of Delivery of Verbal Signals, that continued exposure to the negative phase results in a growing rejection of the negative phase, this suggesting that beneath the individual's self criticism lies a set of positive aspirations which are activated by the continuous repetition of his own self-criticisms.

We wish to stress that in every patient in whom we have produced change in one or in a group of undesirable characteristics, there remains a far greater number of neurotic constellations which we have not attempted to change either because of their sheer number and complexity or because we have not yet developed our procedures to the point where we might deal with such complex matters. (For instance, delayed maturation, or the extensive breakdown in self-stabilizing mechanisms such as found in drug addicts, or the intensely rewarded patterns of the sexual deviant.)

Turning to the durability of results, we recognize that this is affected by multiple factors. For several years we have known that social reinforcement is a major force as described earlier and, that, where it is in full operation, the new trait we have constructed may become permanently incorporated. At the same time, we have become increasingly aware that social acceptance is complex. The phase of re-establishment in extra-mural activity is particularly difficult. The traits which have been built up by exposure to repetition are more commonly inactivated during this phase than at any other time.

In considering the matter, it must be borne in mind that we are constantly responding in terms of long-established patterns to regularly recurring demands from the home, neighbourhood and work situations. We must also recall that in the neurotic patient, not only are certain of his patterns neurotic, but the demands made by some of the figures in his environment are particularly likely to elicit these neurotic patterns. For instance, an excessive dependency in the case of a wife is not infrequently reinforced and perpetuated by over-protectiveness on the part of the husband.

Hence we have found that the patient returning home after new traits have been built up, will respond in a variety of ways depending upon the reactions of his family and his work group to his new characteristics. For example, the impact of the confidence we had built up in one woman was such that her husband was willing to accept in large part the reorganization of their life which she proposed. He gave up a particularly time-consuming job; thus providing more joint social life which was mutually satisfactory, and which in turn reinforced her growing confidence.

In another instance, the wife was able to free herself from the dominance of her mother, friction between herself and her husband on this score was reduced, and a richly satisfactory sexual relationship was established in place of the progressive straying of the husband outside marriage.

In less successful instances, the marital partner accepts the new trait at first (e.g. a normal expression of hostility or an increased sense of adequacy), but later attempts to undermine the new pattern which then becomes less effective and which, because it is being undermined, is the cause of growing anxiety on the part of the patient. At the far end of the scale are those instances where new traits are rejected by the home figures at once. There ensues immediate turmoil on the part of the patient and, ordinarily, the new traits rapidly disappear.

We can say that where there are strong demands in the home and work situations for the old neurotic traits to continue, the results of exposure to repetition of verbal signals are likely to be poor. This is also true where the home situation is highly complex; where the individual goes back to a home where there is not one generation but two or three living under the same roof. Contrariwise, where the home situation is simple, where the spouse is tolerant and capable of constructive adaptation, and where in particular the change produced is one long-sought by both partners, results are good.

Another factor, quite apart from social reinforcement, is the intensity of the impact of the repetition, and here it is most important that the switcher, namely those mechanisms which operate at the symbolic level to prevent conformity to repetition, should have been inactivated as far as possible over the period of exposure. The means of inactivation which we have found most useful are those already recorded, that is, prolonged sleep and electroshock treatment.

Finally, we have recently begun to test the hypothesis first raised by Pavlov and more recently by Eysenck, that individuals vary considerably in the ease with which they take up and maintain new learning. We have as yet reached no final decisions.

SUMMARY

1. Procedures which have been developed to bring about a personality change through exposure to repetition of verbal signals are presented.

2. The results in ten psychoneurotic patients are reported.

3. Repetition is shown to be a powerful force in producing change by mechanisms other than those hitherto recognized.

ACKNOWLEDGMENT

The work on this project was supported by a grant from the Society for the Investigation of Human Ecology, Incorporated.

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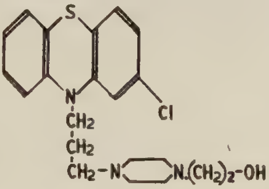
patients. They claimed that 80–100 mg. gave analogous results to 150 mg. of chlorpromazine hydrochloride.

Methopromazine, or 10-(3-Dimethylaminopropyl)-2-methoxyphenothiazine,* was found to have only half the activity of chlorpromazine hydrochloride in a group of 30 patients of unspecified diagnosis. The trial was uncontrolled (Borel, Coiffer and Dechosal, 1957).

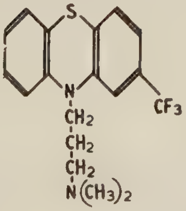
Methotrimeprazine, or 10-(3-dimethylamino-2-methylpropyl)-2-methoxyphenothiazine† was used by Deschamps and Madre (1957) in a small, uncontrolled group of patients. Good results were reported.

Perphenazine



1-[3-(2-chloro-10-phenothiazinyl) propyl]-4-(2-hydroxyethyl) piperazine‡ was employed by Mason-Browne (1957) with chronic psychiatric patients displaying anxiety or over-activity. A double-blind technique was employed. Seventy-five patients were given 48 mg. of perphenazine daily, 75 mg. of chlorpromazine hydrochloride daily or placebo. An anxiety rating scale showed statistically significant improvement in the group receiving perphenazine, but not in the other two groups.

Fluopromazine



10-(3-dimethylaminopropyl)-2-trifluoromethyl-phenothiazine§, was compared (100–800 mg. daily) with trifluoperazine (10–120 mg. daily) and with placebo, the drugs being given successively to 47 psychotic patients, mostly chronic schizophrenics. The double-blind technique was used, but no statistical evaluation was attempted. It was concluded that fluopromazine produced tranquillization similar to that of chlorpromazine hydrochloride, but more rapidly (Rudy, Rinaldi, Costa, Himwich, Tuteur and Glotzer, 1958).

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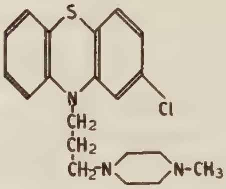
* Mopazine, 4632 RP (Rhône-Poulenc-Spécia), Tentone, CL 22373 (Lederle), Methoxypromazine.

† Veractil (May & Baker), Levomepromazine, 7044 RP (Rhône-Poulenc-Spécia).

‡ Trilafon (Schering), Fentazin (Allen & Hanbury).

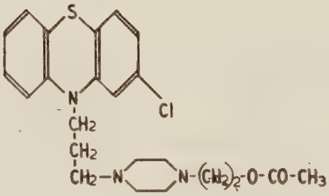
§ Vespral (Squibb, England), Vesprin (Squibb, U.S.A.), MC 4703 (Squibb), triflupromazine.

Prochlorperazine



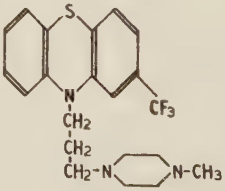
1-[3-(2-chloro-10-phenothiazinyl) propyl]-4-methylpiperazine* was used in a dose of 150 mg. daily given in sustained-release capsules. The study was uncontrolled and poorly planned. Fourteen out of 27 chronic schizophrenic patients were reported as making "good social improvement" (Wilcox, 1958).

Thiopropazate



1-(2-acetoxyethyl)-4-[3-(2-chloro-10-phenothiazinyl) propyl] piperazine† was used by Mathews (1958) in an uncontrolled trial of poor design. Nine out of 15 chronic schizophrenic patients were said to improve. The effective dose was one-third that of chlorpromazine hydrochloride.

Trifluoperazine



2-trifluoromethyl - 10 - [3′ - (4″ - methyl - 1″ - piperazinyl) propyl] phenothiazine‡ has been used by Forrester (1958) in a small, uncontrolled trial with 23 chronic, disturbed patients. Poor results were reported after 4 weeks in a dosage of up to 30 mg. daily.

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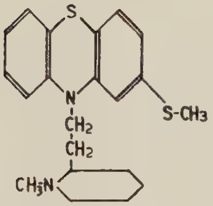
* Compazine (Smith, Kline & French), Stemetil (May & Baker), 6140 RP (Rhône-Poulenc-Spécia), Proclorpémazine (French workers), Témentil.

† Dartalan (Searle), SC 7105.

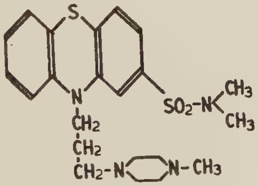
‡ Stelazine (Smith, Kline and French), SKK 5019.

Thioridazine



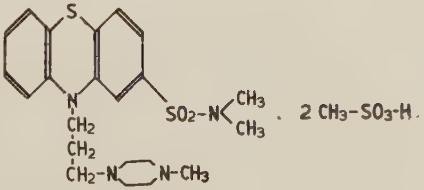
2-methylmercapto-10-[2-(*N*-methyl-2-piperidyl) ethyl]-phenothiazine* was used by Cohen (1958) in an uncontrolled trial in doses of 100–400 mg. daily. He reported that "59 per cent. of 17 schizophrenics improved".

7843 RP(Rhône-Poulenc-Spécia)



Dimethylsulphamido - 2 - (methyl -4″ -piperazinyl - 3′ -propyl) - 10 -phenothiazine†, has been said to produce a "modification of the fundamental temper" of schizophrenia as well as to improve the "superficial symptoms". However, no information was given regarding the data on which these conclusions were based (Perrin, Lambert, Balvet, Brousolle, Berthier, Beaujard, Achaintre, Requet and Revol, 1958).

N, N-dimethyl-10-[3-(1-methyl-4-piperazinyl)-propyl]-2-phenothiazine sulphonamide dimethanesulphonate:



did not further improve 19 chronic schizophrenic patients (who had already been subjected to "phenothiazine and/or milieu" treatment) in an uncontrolled trial (Kurland and Vasconcellos, 1958).

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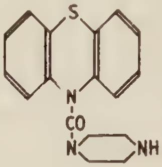
* Melleril (Sandoz), TP-21.

† SKF 5883 (Smith, Kline & French).

5501 MD (Laboratoires Delalande)

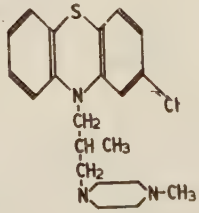


N-thiodiphenyl-carbamyl-piperazine, was used by Fouks, Lainé, Ferrant and Pagot (1959) in doses as high as 1 g. daily. It was found to be "perhaps less active" than other tranquillizers.

Fluphenazine, or 4(-[3-2-(trifluoromethyl)-10-phenothiazinyl]propyl)-1-piperazine-ethanol dihydrochloride*, was found to be effective in an uncontrolled trial involving 110 psychiatric patients. The usual dose was 5–15 mg. daily (Darling, 1959).

Trimeprazine, or 10-(3-dimethylamino-2-methylpropyl) phenothiazine†, was used successfully with 50 psychiatric patients. The trial was uncontrolled and the usual dose was 400–600 mg. daily by mouth (Zoila, Basset and Lebreton, 1959).

6710 RP(Rhône-Poulenc-Spécia)



Chloro-2-(methyl-4″-piperazinyl-1″-3′-methyl-2′-propyl)-10-phenothiazine, was found to be a powerful anti-hallucinatory drug in an uncontrolled trial on 200 psychiatric patients (Achaintre, Lambert, Beaujard, Brousolle, Berthier, Balvet, Requet and Revol, 1959).

PHENOTHIAZINE DERIVATIVES IN THE TREATMENT OF SCHIZOPHRENIA

1. *Chlorpromazine Hydrochloride*

Charatan (1954) found 75–300 mg. daily by mouth ineffective with 22 patients. The group included 14 schizophrenics. No control group was studied. He found that intramuscular administration resulted in clinical improvement.

Vaughan, Lieberman and Cook (1955) report a double-blind trial involving 48 female schizophrenic patients. The group which received chlorpromazine hydrochloride showed greater improvement than the group which received placebo and the difference was significant at the 1 per cent. level.

Baker (1955) claimed that the drug did not remove the patient's disorders of mood or thought. Delusions remained, though the patient was less disturbed by them. Hallucinations sometimes ceased.

Kinross-Wright (1955) did not agree that the basic structure of the psychosis was untouched. He asserted that almost half of 40 paranoid schizophrenics showed remission of all their symptoms.

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* Prolixine (Squibb).

† Théralène (Lab. Théraplix), Panectyl (Poulenc), Alimémazine, 6549 RP (Rhône-Poulenc-Spécia).

Kehoe and Pollard (1956) endeavoured to find the minimal effective dose of chlorpromazine hydrochloride. The average final dose with psychotic patients who improved during the first five weeks of treatment was 160 mg. a day, whereas that of those improving during the subsequent seven weeks was 266 mg. a day. This would seem to indicate that the effective dose is much lower than other published reports would suggest. The investigation was not controlled and there was no statistical treatment.

Denber and Bird (1957) reviewed 1,523 patients, including 1,040 cases of dementia praecox, treated with chlorpromazine hydrochloride. The patients who showed the best results required relatively low doses. If control was not established with 600 to 900 mg. daily, higher doses did not influence the results. They point out that English workers seldom use more than 400 mg. a day, whereas American, French and Swiss workers use up to 1,000 mg. a day and more.

Feldman (1957) reports that of 317 patients put on chlorpromazine hydrochloride in 1954, 32 were out of hospital at the end of the first year and 83 (72 per cent. schizophrenics) were out at the end of the second year; 66·5 per cent. of the latter group were still taking the drug.

Abrams (1958) compared chlorpromazine hydrochloride (18 patients) with a placebo which was identical in size, shape and colour (16 patients). The patients were all chronic, female schizophrenics. After four months there was a statistically significant difference in favour of chlorpromazine hydrochloride in the rating scale score (Multidimensional Scale for Rating Psychiatric Patients). No significant difference was found as regards intelligence quotient, anxiety, hostility or withdrawal.

Vasconcellos and Kurland (1958) used a sustained release form of the drug (the "Spansule" preparation made by Smith, Kline & French). They found that patients could be maintained on a single morning dose of half their previous daily total.

Delay, Deniker, Ropert, Beek, Barande and Eurieult (1959) claim that the therapeutic effect of chlorpromazine hydrochloride is to produce akinesia. In contrast, reserpine and prochlorperazine are said to produce hyperkinetic symptoms.

Vaughan, Lieberman and Cook (1955) report that all of 72 schizophrenic patients who had improved with chlorpromazine hydrochloride relapsed within three months when a placebo was substituted.

Brooks (1959) reported the effects of suddenly substituting an inert placebo for chlorpromazine hydrochloride in female patients who had been receiving the latter for eighteen months and longer. Acute withdrawal symptoms occurred during the first ten days—tension, restlessness, muscular pains and insomnia. A few of the patients developed severe vomiting. By the tenth day these symptoms had subsided, but the patients were as disturbed as they had been prior to their receiving chlorpromazine hydrochloride. It should be noted that many of these supposed withdrawal symptoms may occur with placebo medication alone (Hollingworth, 1912).

2. *Pecazine*

Thorpe and Baker (1956) assigned 48 deteriorated, female, schizophrenic patients to four groups on the basis of alternate admissions. Chlorpromazine hydrochloride and pecazine were given respectively to two of the groups, 150 mg. daily for two weeks then 300 mg. daily for a further two weeks. The remaining two groups received placebo or no medication. The trial was blind. After four weeks of treatment the mean score on a scale measuring deterioration was almost significantly better for the chlorpromazine group than for the others.

The chlorpromazine group showed a significantly better mean tension score than the placebo and control groups, whereas the pecazine group was significantly better than the placebo group only.

Baker and Thorpe (1957) found that pecazine did not significantly reduce daytime incontinence in deteriorated psychotic patients. The trial was controlled and blind.

3. *Promazine*

Fleming, Spencer and Whitelaw (1959) conducted a double-blind trial with 51 disturbed, chronic, female, schizophrenic patients. The patients were given chlorpromazine hydrochloride or promazine, 300 mg. daily by mouth, or placebo. Chlorpromazine hydrochloride produced significantly better results than the placebo, whereas promazine did not.

Gilmore and Shatin (1959) carried out a double-blind trial with 37 acute schizophrenic patients. They were given chlorpromazine hydrochloride or promazine, 400 mg. daily, or placebo, by mouth. The trial lasted 31 days. Chlorpromazine hydrochloride was significantly more effective than promazine and placebo ($P=0\cdot001$), whereas promazine was not significantly more effective than the placebo.

4. *Acepromazine*

Simpson (1958) found acepromazine deleterious to 47 chronic schizophrenic patients. The trial was uncontrolled.

5. *Methopromazine*

Gosline, Walters and Saunders (1959) found this drug less effective than other phenothiazine derivatives in the treatment of acute schizophrenia. High doses (900–1,200 mg. a day) were employed. The trial was uncontrolled.

6. *Methotrimeprazine*

In a double-blind but uncontrolled trial on 24 deteriorated, female, schizophrenic patients, chlorpromazine hydrochloride (in a mean daily dose of 349·8 mg.) was compared with methotrimeprazine (mean daily dose 216·5 mg.). The trial lasted 20 weeks. Both groups of patients showed significant improvement of mean rating scale score above the score before treatment. There was no significant difference between the groups (Baker and Thorpe, 1958).

7. *Perphenazine*

Reference has been made to the double-blind trial conducted by Mason-Browne (1957), who found that a group of chronic psychiatric patients on perphenazine showed a statistically significant improvement (anxiety rating scale score), whereas groups on chlorpromazine hydrochloride and placebo did not.

8. *Fluopromazine*

Hanlon, Kurland, Esquibel and Ota (1958), in a double-blind trial involving 32 chronic, female, psychotic patients, subjected each patient in turn to chlorpromazine hydrochloride, placebo and fluopromazine for unequal periods. The mean dose of chlorpromazine hydrochloride was approximately 240 mg. a day and the dose of fluopromazine about half as great. The mean rating scale score showed no significant change between the ends of the chlorpromazine and placebo periods. A statistically significant improvement occurred between the ends of the placebo and fluopromazine periods. Estimates of the patients' withdrawal showed little change.

Walsh, Walton and Black (1959), in a double-blind trial on 66 chronic, female, schizophrenic patients, in which matched groups were employed, found that neither fluopromazine nor chlorpromazine hydrochloride were more effective than a placebo in causing improvement as measured by the Rowell Graphic Behavioural Rating Scale and the Venables Rating Scale for activity withdrawal. All three drugs were associated with considerable improvement, but the differences were not statistically significant.

9. *Prochlorperazine*

Dransfield (1958) conducted a double-blind, controlled trial with 50 aggressive, disturbed, chronic, male, psychiatric patients. Forty-six schizophrenic patients were included. Two matched groups were given placebo initially, then chlorpromazine hydrochloride in the case of one group and prochlorperazine in the case of the other. The maximum daily doses were 300 mg. and 150 mg. respectively. Both drugs were associated with improvement. There was no significant difference between the two groups, but the method of assessment was rather crude. The absence of a control group also detracted from the value of this investigation. This worker found no support for the view that the best clinical results are obtained when Parkinsonism occurs.

King and Weinberger (1959) conducted a double-blind trial with chronic schizophrenic patients, 27 males and 45 females. One group was given prochlorperazine 100 mg. daily, a second group chlorpromazine hydrochloride, 400 mg. daily and a third group lactose placebo. After ten weeks of treatment, all three groups had improved significantly, but there was no significant difference between the groups.

COMPARISON OF CHLORPROMAZINE HYDROCHLORIDE WITH OTHER FORMS OF TREATMENT IN SCHIZOPHRENIA

1. *Barbiturates*

Little (1958), in a satisfactorily controlled, double-blind trial, found no significant difference between the clinical effects of chlorpromazine hydrochloride 150 mg. daily, amylobarbitone 400 mg. daily and placebo, when these were given in turn to 152 chronic psychotic patients with a variety of diagnoses. One hundred and nine schizophrenic patients were included. The patients had three weeks on each drug. Assessment was on a rather insensitive, 7-point scale of clinical progress and the patients continued to take other sedatives (often barbiturates) during the trial.

2. *Reserpine*

Freeman, Arnold and Cline (1956) describe a trial in which a double-blind technique was employed, but in which the two treatment groups were not comparable, one group consisting of lobotomized males and the other of non-lobotomized females. The former received chlorpromazine hydrochloride or placebo, the latter reserpine or placebo. The active drugs produced greater improvement than the placebo only when used in high dosage. Only 39 patients were involved, all of them schizophrenics.

Kurland (1956) treated 200 female schizophrenic patients with 3–6 mg. of reserpine daily and a further 200 with 200–400 mg. of chlorpromazine hydrochloride daily. The trial was not blind and no statistical evaluation was attempted. Four per cent. of the patients having reserpine and 9 per cent. of those having chlorpromazine hydrochloride were rated as showing marked improvement.

Shepherd and Watt (1956) studied 24 deteriorated, apathetic, female, schizophrenic patients. These were given reserpine 10 mg. daily, chlorpromazine hydrochloride 300 mg. daily and placebo, in varying orders, each drug for 6 weeks. A double-blind technique was employed, and the patients were rated on a seven-point scale. Comparing the improvement obtained on the different drugs, χ^2 was found to be $18 \cdot 4$, which—for four degrees of freedom—gives $P < 0 \cdot 002$. The order of efficacy was chlorpromazine hydrochloride, placebo, reserpine. Side-effects were more common with reserpine.

Barrett, Ellsworth, Clark and Ennis (1957) employed a double-blind technique in a trial involving 30 chronic schizophrenic patients. Drugs were given in identical capsules. The patients were given placebo for two months then reserpine, chlorpromazine hydrochloride or a combination of the two for three months. The numbers of patients improving in the three groups of ten were as follows: 7 on the combination, 5 on chlorpromazine hydrochloride and 3 on reserpine.

Tuteur, Stiller and Whitehill (1957) found chlorpromazine hydrochloride to be more effective than reserpine or a combination of the two drugs. Side-effects were very much the most frequent with the combination and least frequent with chlorpromazine hydrochloride. The trial was poorly planned, non-blind and uncontrolled.

These results leave little doubt that chlorpromazine hydrochloride is the more effective drug.

3. *Insulin Coma Therapy*

Boardman, Lomas and Markowe (1956) assigned a hundred schizophrenic patients to two groups on the basis of alternate admissions for each sex separately. Acute catatonic patients were excluded. In one group the patients were given 50 insulin comata each and in the other oral chlorpromazine hydrochloride, up to 300 mg. daily. No rigid scheme of dosage or duration was adopted and a double-blind technique was not attempted. The patients were assessed on a five-point symptom scale. Both groups improved, but the chlorpromazine group improved more. The difference was significant at the 5 per cent. level. These workers estimated the mortality in insulin coma therapy as $0 \cdot 50$–$1 \cdot 29$ per cent. They pointed out that it is much lower with chlorpromazine hydrochloride.

4. *Electrical Convulsion Therapy*

Electrical convulsion therapy, given twice daily for 22 treatments, resulted in a statistically significant deterioration in 20 chronic, male, schizophrenic patients. Chlorpromazine hydrochloride, 300 mg. daily, produced a significant improvement in a matched group of twenty patients. The investigation was controlled but not blind (King, 1958).

INDICATIONS FOR THE USE OF PHENOTHIAZINE DERIVATIVES

There have been several attempts to discover the type of case most likely to respond to phenothiazine derivatives.

Rathod and Rees (1958) found that the response of the systolic blood pressure to methacholine chloride was correlated with clinical improvement on chlorpromazine hydrochloride, whereas the response to intravenous adrenaline was not.

Kehoe and Pollard (1956) postulated that individual differences in response to chlorpromazine hydrochloride might be due to the balance between the parasympathetic and sympathetic systems in the production of anxiety.

Baker (1955) asserted that the more destructive and aggressive the patient, the more likely he was to respond to chlorpromazine hydrochloride. Affective flattening was little affected and somatic delusions were made worse.

Denber and Bird (1957) found no relationship between the diagnostic sub-group of dementia praecox and the response to chlorpromazine hydrochloride.

Cares, Asrican, Fenichel, Sack and Severino (1957) collated the results obtained with 3,014 patients treated in hospital by chlorpromazine hydrochloride. Patients were rated "good", "fair" or "no change" according to their clinical response. They report the following results:

270 catatonics — 82 per cent. improved.
336 hebephrenics — 79 per cent. improved.
464 paranoid schizophrenics — 84 per cent. improved.
21 simple schizophrenics — 80 per cent. improved.
43 juvenile schizophrenics — 74 per cent. improved.

No statistical analysis is included in their paper. If the sub-groups (excluding the juvenile group) are compared by means of the χ^2 test, a value of χ^2 of $3\cdot157$ is obtained, giving $P>0\cdot30$ for three degrees of freedom. Comparing the sub-groups which differ most, χ^2 is $2\cdot55$, giving $P>0\cdot10$ (one degree of freedom). There was, therefore, no significant difference between the four sub-groups.

These results are of great interest, as controlled trials do not usually include sufficient numbers in each sub-group for conclusions to be reached on this point.

Nicoletti and Magherini (1957) describe a study in which fifteen schizophrenic patients were given reserpine, seventeen were given reserpine and choline and thirty-two were given chlorpromazine hydrochloride and choline. Various features of each patient's history, symptomatology and therapeutic response were given numerical values after six months of treatment. Factorial analysis revealed two common factors, a factor of schizophrenia and a second factor. One group of patients—described as the "hebephrenic-dementing group"—showed a high saturation with this second factor. The other group—the "paranoid group"—showed a low saturation. The paranoid group showed a significantly greater susceptibility to therapy with chlorpromazine hydrochloride and choline or reserpine and choline. These two groups would seem to correspond to Kallmann's nuclear and peripheral groups respectively, which were delimited on genetical grounds (Kallmann, 1938).

Little (1958) found that psychotic patients who showed a satisfactory response to amylobarbitone tended to do so to chlorpromazine hydrochloride also.

Blair and Brady (1958) claim that chlorpromazine hydrochloride is less effective with male than with female patients.

Mead, Ellsworth and Grimmett (1958) found that apathetic schizophrenics showed the poorest response to chlorpromazine hydrochloride. All diagnostic sub-types were represented in this group. These workers report a double-blind trial involving some 32 male patients of this type. They claim that their results support the hypothesis that such patients will respond to chlorpromazine hydrochloride only if tension is first induced by means of ephedrine. Their figures, however, give no statistical justification for such a conclusion.

Although there are some indications for the use of the drug in schizophrenia, they are by no means clear-cut and any schizophrenic patient may respond. Paranoid or aggressive patients appear to respond well on the whole and apathetic patients poorly, but with individual patients only a clinical trial can determine whether or not a satisfactory response will occur.

UNDESIRABLE SIDE-EFFECTS AND COMPLICATIONS

The choice of drug in a particular case must be dictated partly by its clinical effectiveness but also partly by the incidence of side-effects and complications. An exhaustive account would be out of place here. In practice, the side-effects the incidence of which will have to be taken into account are the Parkinsonian syndrome, drowsiness and gain of weight. The frequency of serious complications—jaundice and agranulocytosis—will also have to be considered.

A table is appended giving the incidence of these according to various authorities. The number of patients given the drug is also quoted for each authority.

A few generalizations may be made. The following drugs, when used in their therapeutic range of dosage, produce a higher incidence of Parkinsonian symptoms than chlorpromazine hydrochloride:

Perphenazine
Fluopromazine
Prochlorperazine
Thiopropazate
Trifluoperazine
7843 RP
Fluphenazine
6710 RP

Information about the incidence with the other drugs is inadequate.

The following show a greater incidence of jaundice than does chlorpromazine hydrochloride:

Pecazine
Acepromazine
7843 RP

TABLE

Incidence of Side-Effects and Complications (Percentages)

Drug and Authority	Parkinsonian Syndrome	Drowsiness	Gain of Weight	Jaundice	Agranulocytosis
Chlorpromazine hydrochloride:					
Winkelman, 1957 (1,005 patients)	0·2	83	13·5	0·81	0
Denber and Bird, 1957 (1,523 patients)	7·6	—	—	1·2	0
Cares *et al.*, 1957 (1,534 patients)	1·7	—	—	0·6	—
Goldman, 1958 (847–1,227 patients)	0	4·3	35	0·4	0·33
De Nosaquo, 1956 (4,000,000 patients)	—	—	—	—	0·001–0·002
Kinross-Wright and Moyer, 1956 (10,909 patients)	—	—	—	1·4	—
Pecazine (various):		occurs	occurs		
Mitchell *et al.*, 1957 (37 patients)	—	—	—	5·4	—
Werenberg, 1955 (100 patients)	—	—	—	—	1
Promazine (various):			60	occurs	occurs
Azima and Durost, 1957 (159 patients)	—	5·7	—	—	—
Piperidinochlorphenothiazine:					
Malitz and Hoch, 1956	—	occurs	—	—	—
Acepromazine:					
Ferguson, 1958 (50 patients)	—	50	—	6	—
Methopromazine:					
Gosline *et al.*, 1959 (29 patients)	3·5	6·9	—	—	—
Methotrimeprazine (various):			0		
Webber, 1958	—	—	—	—	1 case
Perphenazine (various):	28				
Darling, 1958 (75 patients)	54·7	—	—	—	—
Goldman, 1958 (206–207 patients)	22·8	1·9	5·8	0	0
Fluopromazine:					
Goldman, 1958 (176–180 patients)	17	1·1	2·2	0	0
O'Brien and Anderson, 1959 (100 patients)	0	25	—	—	—
Walsh *et al.*, 1959 (600 patients)	12	—	—	—	—
Prochlorperazine (various):	20				
Dransfield, 1958 (25 patients)	44	68	—	0	—
Goldman, 1958 (640–667 patients)	37·7	2·9	8·1	0	0
Thiopropazate:					
Mathews, 1958	almost all	—	—	0	—
Trifluoperazine:					
Forrester, 1958 (25 patients)	28	occurs	—	—	—
Kruse, 1959 (110 patients)	81·8	—	—	—	—
Thioridazine:					
Cohen, 1958	0	occurs	—	—	—
Delay, Pichot *et al.*, 1959 (35 patients)	5·7	—	—	—	—
7843 *R.P.:*					
Delay, Deniker *et al.*, 1959 (38 patients)	87	occurs	—	—	—
Denber *et al.*, 1959 (23 patients)	56·6	34·8	—	4·3	—
N,N-dimethyl-10-[3-(1-methyl-4-piperazinyl)-propyl]-2-phenothiazine sulphonamide dimethanesulphonate:					
Kurland and Vasconcellos, 1958 (19 patients)	26	—	—	—	—
5501 MD:					
Fouks *et al.*, 1959	0	—	—	—	—
Fluphenazine:					
Darling, 1959 (110 patients)	31·8	9·1	—	—	—
Trimeprazine (various):		occurs			occurs
Zoila *et al.*, 1959 (50 patients)	—	—	—	—	—
6710 RP:					
Achaintre *et al.*, 1959 (200 patients)	13	1·5	—	—	—

Jaundice has also occurred with promazine, but has not been reported with the others.

Agranulocytosis has so far been recorded with:

Chlorpromazine hydrochloride
Pecazine
Promazine
Methotrimeprazine
Trimeprazine

SUMMARY

The first use of chlorpromazine hydrochloride in mental illness was reported in France in 1952. Subsequently a variety of other phenothiazine derivatives have been introduced into psychiatry:

Pecazine (1955)
Promazine (1956)
Piperidinochlorphenothiazine (1956)

Acepromazine (1957)
Methopromazine (1957)
Methotrimeprazine (1957)
Perphenazine (1957)
Fluopromazine (1958)
Prochlorperazine (1958)
Thiopropazate (1958)
Trifluoperazine (1958)
Thioridazine (1958)
7843 RP (1958)
N, N-Dimethyl-10-[3-(1-methyl-4-piperazinyl)-propyl]-2-phenothiazine sulphonamide dimethanesulphonate (1958)
5501 MD (1959)
Fluphenazine (1959)
Trimeprazine (1959)
6710 RP (1959)

Several controlled trials have confirmed the usefulness of chlorpromazine hydrochloride in schizophrenia. Most of these trials have involved chronic patients.

Some of the other drugs have been compared with chlorpromazine hydrochloride from this point of view. Considering only evidence from double-blind trials, the following appear to be more active than chlorpromazine hydrochloride, when used in their therapeutic range of dosage (a somewhat vague proviso):

Perphenazine
Fluopromazine

The following appear to have comparable activity to chlorpromazine hydrochloride:

Methotrimeprazine
Prochlorperazine

and the following to be less effective:

Pecazine
Promazine

There is some less satisfactory evidence that acepromazine and methopromazine are also less active than chlorpromazine hydrochloride. It should be noted that these observations refer to optimal therapeutic activity and not to weight-for-weight activity.

Information about the remaining ten compounds is inadequate.

Complementary to the discussion of the relative clinical efficacy of these drugs is the consideration of the relative incidence of side-effects and complications. When used in their therapeutic dosage, the following drugs produce a higher incidence of Parkinsonian symptoms than does chlorpromazine hydrochloride:

Perphenazine
Fluopromazine
Prochlorperazine
Thiopropazate
Trifluoperazine
7843 RP
Fluophenazine
6710 RP

The following show a greater incidence of jaundice than does chlorpromazine hydrochloride:

Pecazine
Acepromazine
7843 RP

Jaundice has also occurred with promazine, but has not been reported with the others.

Agranulocytosis has so far been reported with:

Chlorpromazine hydrochloride
Pecazine
Promazine
Methotrimeprazine
Trimeprazine

In short, there is no indication at present that any of these drugs could usefully replace chlorpromazine hydrochloride. In those rare cases where jaundice or agranulocytosis has occurred with chlorpromazine hydrochloride, fluopromazine would seem to be indicated.

There is clear evidence that chlorpromazine hydrochloride is more effective than reserpine in chronic schizophrenia, and a moderately satisfactory—though not blind—trial has suggested that it is more effective than insulin coma therapy in acute schizophrenia (Boardman, Lomas and Markowe, 1956).

In the present state of our knowledge, only a clinical trial can determine whether or not a given schizophrenic patient will respond to chlorpromazine hydrochloride.

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ELECTROCOAGULATION OF THE CEREBRAL ORBITAL PROJECTION IN THE PERSISTENT DEPRESSIVE PSYCHOSES OF THE ELDERLY

By

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THE tranquillizing drugs are used so extensively in the control of psychotic states that the wave of enthusiasm threatens to swamp the entire therapeutic field. Yet, until the scope and limitations of these drugs have been established it would be unwise to neglect advances in other methods of treatment. Prefrontal leucotomy has long since passed the crest of its wave, and in recent years conservative operative techniques and a more selective field of clinical application have rendered it a valuable treatment for certain groups of patients.

The earlier standard operation with its blind surgical approach and uncertain side-effects has rightly been discarded, as also the use of brain surgery in schizophrenia, since the best that can be achieved is a one-third discharge rate, and Robin (1958) has shown in a follow-up study of 91 cases with controls that no advantage could be found for the standard leucotomy operation.

Yet it is recognized that leucotomy achieves its best results in the disorders of affect (Pool, 1957) particularly when intractable emotional excesses such as tension, anxiety, agitation and depression dominate the patient. On the other hand, manic states, hypochondriasis and the manic-depressive psychoses show results from leucotomy little better than those for schizophrenia and it is doubtful if the operation has any place in their treatment (Robin, 1958).

The most gratifying results from leucotomy have been found in the severe and intractable depressions of the elderly and senile patient (Scoville and Ryan, 1955; Thorpe, 1958, 1959) and it is in this group of cases that a modified leucotomy procedure with its reduced risk of adverse personality change offers the patient the best chance of recovery.

With the development in recent years of the restrictive leucotomy techniques, encouraging reports have been received on a number of modifications under trial, although more statistical evidence is required to assess their relative efficiency. The recent reviews of Pool (1957), Freeman (1958) and Falconer and Schurr (1959) indicate the variety of procedure (topectomy, cortical undercutting, bimedial and orbital leucotomy) designed to isolate the orbital cortex of the frontal lobes with consequent alleviation of disorders of the affect and minimal personality defect.

A modified leucotomy procedure which seems to have been little explored is the electrocoagulative method introduced by Grantham (1951), and, as we have been unable to find any other reference to its trial in Great Britain, we decided to record our satisfactory experience of this method in the treatment of intractable melancholic states. This operation produces destructions of the ventro-medial fibre tracts by the insertion under X-ray control of an insulated needle through ventral burr holes, and passing a coagulative current. A small discrete tissue lesion is produced at the tip of each needle, and the advantages claimed for the method are more precise localization with minimal damage to the cortex, absence of post-operative convulsions, little or no intellectual impairment, less personality change, and no urinary incontinence.

In the present study we have assessed the results of a Grantham operation on 100 cases of persistent depressive psychosis treated at the Middlewood Hospital. The criterion of operation in the series was intractable or repeated relapsing severe depressions in patients showing no sustained improvement from other acceptable forms of treatment including electroplexy. After excluding 3 schizophrenics, the remaining 100 were consecutive operations performed during the 5-year period 1952 to 1957 by Mr. James Hardman in the Neurosurgical Department of the Sheffield Royal Infirmary. There were 71 females and 29 men in the group, and all (except 8 with retardation) had severe agitated depressions with involutional melancholia predominating, 73 patients being over the age of 50. A diagnostic classification is shown in Table I.

Operative Procedure

After shaving the head and premedicating with "Omnopon" and scopolamine, a vertical incision 7 cm. above the gabella is made under local analgesia

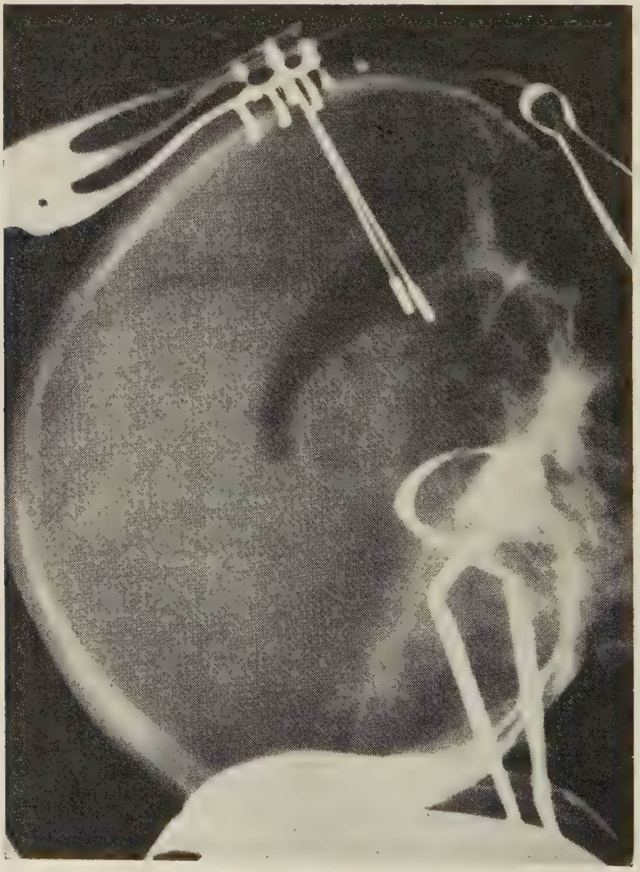

Fig. 1.—Lateral X-ray of skull showing electrodes in correct position.

TABLE I

Diagnostic Categories

Diagnosis	No. of Cases	Improvement Marked	Improvement Mod.	None	Readmitted
Chronic Depressive	46	23	20	3	4
Recurrent "	37	21	16	–	5
Hypochondriacal "	10	3	6	1	3
Obsessional	7	5	2	–	–
	100	52	44	4	12

2½ cm. on either side of the midline, just behind the hair line. Burr holes are made, the dura mater incised, and with the head accurately positioned, a canula is inserted into the anterior horn of each ventricle and about 20 c.c. of fluid removed and replaced by air.

The electrodes are thin steel rods insulated with polythene except for 9 mm. at the tip, and are inserted vertically into the brain, directed slightly backward to a depth of 5·5 cm. placing their tips just in front and below the anterior horns of the ventricles. The patient is carefully, and without head movement, wheeled on the operating table into the adjoining X-ray room.

Lateral and antero-posterior films are taken (Figs. 1 and 2) and if the

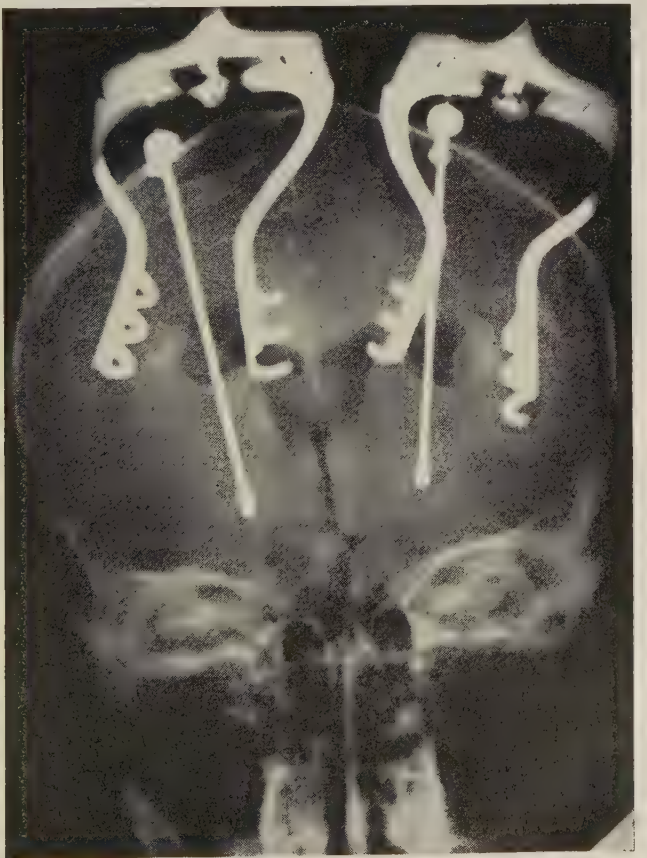

FIG. 2.—Antero-posterior X-ray showing electrodes in correct position just lateral to the anterior horns of the lateral ventricles.

electrodes are seen to be in a satisfactory position, or after changing their position if necessary, the diathermy (Davis-Bovie Automatic-gap Electrosurgical Apparatus) is attached to each in turn and with a power setting of 20 on the coagulation device, the current is passed for 30 sec. and repeated after withdrawal of the electrodes by 1 cm. The optimum current strength is determined by trial in cases of terminal carcinoma with the object of producing an electrocoagulative lesion about 1½ cm. diameter in the inferior medial quadrant of the frontal lobe, just above the medial orbital gyrus (Fig. 3). Such a lesion will interrupt the orbital fibres of the thalamo-frontal bundle at the site of maximal concentration near the anterior limb of the internal capsule.

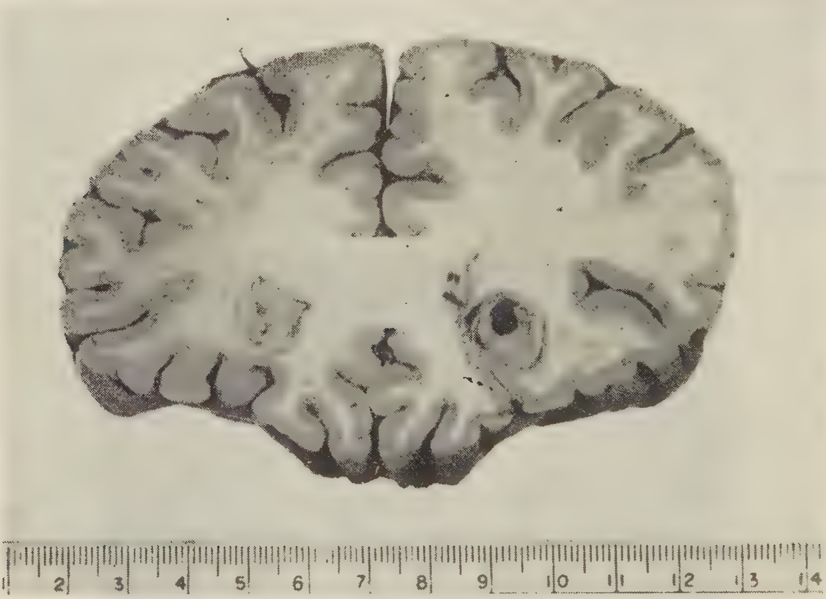

FIG. 3.– Coronal section of the frontal lobes of the brain to show position of electrocoagulative lesions in the orbital segments.

The patient is conscious throughout the operation which, because of the X-ray procedure, takes about 45 min. to complete. During most of the time the anaesthetist maintains a reassuring conversation with the patient, encouraging him to keep his head still. Immediately after the operation there is a noticeable relaxation, and he rests quietly with eyes closed, responding to simple questions, and may exhibit some disorientation.

Post-operative Course

The patient arrives back in the ward in a calm and tranquil state of mind and with little recollection of the operation except in some cases when the feel and sound of the drill is remembered. A few patients express denial of the operation for the first 24 hours. A rise of temperature up to 100° to 101° develops in about 8 hours, and may persist for 2 or 3 days, and seems to be in proportion to the extent of the operative lesion. The observation made by Ayd (1956) that absence of temperature forecasts a poor therapeutic result might be due to minimal lesions, but we have been unable to confirm this in our series.

It is customary to give prophylactic cover of penicillin for the first 3 or 4 days, but there is usually no marked alteration in pulse or blood-pressure, and ordinary soft diet can be taken. The patient can sit up on the second day, get out of bed on the third day when the sutures are removed, and then allowed to be up in the ward. Mental improvement becomes apparent on the first day, agitation disappears, a placid demeanour, a ready smile, and occasionally a short phase of euphoria supervenes. Mental improvement quickly becomes stabilized, and it has been our practice to discharge patients home after three weeks, believing with Freeman that it is the function of the family to rehabilitate him and shape his convalescence. The operation scar is just behind the hair line, and has little adverse cosmetic effect. Many patients develop a moderate increase in weight.

GENERAL RESULTS

The 100 cases have been reviewed and results assessed at the end of 1958, two to seven years following operation. Contact was made in the clinics, in the homes, and when personal interview was impossible, a report by letter was obtained. Only 4 patients could not be traced, having left their previous address, and assessment was based on their last home report (all recovered). Table II shows a summary of the results arranged according to age groups.

TABLE II

Results in 100 Cases of Grantham Leucotomy
1952—1956

		PROGRESS					1958 Review			
Age	No. of	Improvement			Discharged		Deaths		In	At
Groups	Cases	Marked	Mod.	None	No.	Readm.	Operative	Other	Hospital	Home
20-29	2	1	1	–	1	–	–	–	1	1
30-39	8	4	4	–	8	1	–	1	–	7
40-49	17	10	6	1	14	–	–	1	3	13
50-59	26	14	11	1	24	3	1	5	3	17
60-69	32	17	14	1	28	6	1	5	3	23
70-79	15	6	8	1	12	2	1	7	3	4
Total	100	52	44	4	87	12	3	19	13	65

The improvement rate was 96 per cent., including 52 recoveries and 44 moderate improvements. There were 87 patients discharged home. The term "moderate improvement" is used when tension and depression is mitigated, social improvement maintained, with less dependence on others though still retaining traces of the pre-operative symptoms, hypochondriasis especially. Of the 44 moderately improved patients, 32 were discharged home. The only unimproved patient was a female aged 63, who had persistent cephalgia uninfluenced by two Grantham procedures, though her depression was minimal.

Readmissions in relapse occurred in 12 per cent., 3 cases being subsequently discharged and of the 9 remaining one is dead, 7 are moderately improved and 1 (mentioned above) is unimproved. All the readmissions occurred in the moderately improved group, and 8 of them had experienced recurrent depressions before operation. Late depressive relapses occurred in 2 patients following discharge, one committing suicide and the other recovering without readmission.

The operative deaths were 3 in number, 2 from cerebral haemorrhage in hypertensive patients, aged 58 and 70, their deaths occurring on the 9th and 7th post-operative days respectively. A third patient, age 67, died on the 11th day with a purulent basal meningitis.

In a long-term study it is to be expected that many elderly patients will have died from non-operative causes, and at the time of assessment 19 such deaths had occurred, 17 from cardiac or cerebral vascular causes, 1 from cancer and 1 from suicide. Table II shows the deaths to be in the upper age groups, and of the 17 deaths 4 occurred within 1 year, increasing to 10 in 2 years, 12 in 3 years, 14 in 4 years, 16 in 5 years and one more in the sixth year.

Post-operative Complications

There were no instances of urinary incontinence. Epileptic fits occurred in 2 patients, a male aged 60 having one fit on the 6th day and none during the ensuing 2½ years of mental improvement, and the other, a female aged 66, developing late epilepsy after discharge home and reported to have occasional fits.

Some patients complained of tiredness and lack of energy, but nevertheless seemed to do a reasonable amount of work. Outspokenness and free use of criticism is not infrequently noticed by relatives, who should be warned of its possible occurrence. "I can stand up for myself now" a wife said, and the husband of another patient said his wife had never called him a b— before but he didn't mind as she was so much better. If marital incompatibility has been an adverse environmental factor, the post-leucotomy patient may be better equipped to endure the stress, but lack of restraint may cause trouble. One such woman with an unhappy marriage recovered from a chronic depressive suicidal state following leucotomy, but 3 years after discharge was convicted of attempting to poison her husband.

It is doubtful, however, if any serious adverse personality changes can arise from the limited operative lesion produced by the Grantham procedure, and such has been our general impression from the study of this series of cases.

ANATOMICAL STUDY

We were able to make a macroscopic examination of the brain in 4 cases of this series. In the 2 deaths from cerebral haemorrhage the brain showed a large unilateral operative intracerebral haematoma in each case, situated at the site of the coagulative lesion and rupturing into the lateral ventricle. The cerebral arteries showed atherosclerosis. In the third case the post-operative infection had progressed to a purulent basal meningitis though the operative lesions were satisfactory.

The fourth brain available for study came from a female aged 72 who died in hospital 2 months after a successful orbital leucothermy. Although relieved of her chronic depressive psychosis, she died of coronary thrombosis. Examination of the brain in coronal slices showed what we would regard as a typical Grantham electrolytic lesion situated in the optimum position in the orbital white matter (Fig. 3).

The following is an abstract of the report from the neuro-pathologist. The illustration shows the post-mortem coronal section of the brain at a plane 4 cm. behind the tip of the frontal poles. The two small areas of coagulation necrosis are situated in the lower medial quadrants of the white matter. They are roughly 1 cm. in diameter on the left side and 1·2 cm. in diameter on the right side. The area on the right side extends into the deeper layers of the cortex in the depths of a sulcus. On this side the lesion is situated just below and lateral to the tip of the anterior horn of the right lateral ventricle. A further coronal section 1 cm. posterior to the first cut at the tip of the temporal pole shows the area of coagulation necrosis in the lower medial quadrant at the ventral extremity of the anterior limb of the internal capsule. The area involved extends into the ventro-lateral part of the head of the caudate nucleus. At this level the lesions are again 1 cm. in diameter.

The lesion on the right side is slightly larger than that on the left and extends into the anterior part of the lenticular nucleus. Its ventral extremity extends into the cortex of the medial and central inferior frontal convolutions, and the middle cerebral artery can be seen in the sylvian fissure less than ½ cm. away from the limit of the area of coagulation.

Discussion

Many neurosurgical procedures at present under trial are directed at the frontal lobes with the object of relieving intractable disorders of the affect by interruption of the thalamo-frontal fibres. Most surgeons now appear to have as their anatomical target the isolation of the orbital cortex which MacLean (1949) and Fulton (1951) regarded as the cortical representation of the so-called "visceral brain", under which is comprehended the posterior orbital cortex, the cingulate gyrus, temporal pole, hippocampus, amygdaloid nucleus and their connections with each other, and with the hypothalamus and thalamus (Meyer and Beck, 1954).

The problem for the surgeon is to combine maximal therapeutic effect with minimal operative risk, and avoidance of unnecessary destruction of brain tissue with its resultant adverse personality changes. There has been a high measure of achievement in this direction, and the overall results of the different procedures compare well with each other although the published reports are too few to give a clear result.

Each neurosurgeon develops the technique of his choice, there being a choice between the open operation such as topectomy by Pool (1955), orbital undercutting by Scoville (1953), Tow and Lewin (1953), Strom-Olsen and Northfield (1955), Knight and Tredgold (1955), Hirose (1958) or bimedial leucotomy by Greenblatt and Solomon (1952), Falconer and Schurr (1959), and the closed operational approach as in the transorbital leucotomy of Freeman (1952), the blind rostral leucotomy of McKissok (1958) the former lower quadrant leucotomy of Thorpe and Hardman (1952) and the electro-coagulative method of Grantham (1951).

The Grantham operation was originally used for the relief of intractable pain and only later extended into the field of psychiatry. Few publications of any magnitude have so far appeared, but favourable reports have come from Grantham (1953, 1956), McIntyre (1954), Soupault (1955), and Ayd (1956, 1957). The advantages of the Grantham technique as a closed operation are the anatomical accuracy obtained by X-ray visualization of the electrodes during operation, the wide measure of control in the position and size of the lesion produced, the easy repetition of the operation at the same or a different level and the absence of any need for a general anaesthetic. It is particularly suitable for older or debilitated patients.

We adopted the operation for routine use in 1952 and have not found any reason to change. The operative risks are minimal though a 2 per cent. cerebral haemorrhage is not unexpected in view of the many elderly patients with cerebral atherosclerosis. Post-traumatic epilepsy was negligible since the only one persistent case could be due to cerebral vascular disease. Personality defects have been few, outspokenness being a prominent feature in some 20 patients of the series.

Some comments on the Grantham operation have been made by other investigators, including Pool (1957), who states that in his experience the results are somewhat unpredictable unless the effects of cauterization are tested during the operation. Freeman (1958) considers the procedure too recent to permit adequate clinical or anatomal studies that would establish its superiority over other methods with a larger period of performance behind them. Ferey et al (1956) found a variability in the position of the lesions in their two brain specimens. None of these comments is serious, and much depends upon the skill and experience of the operator.

The therapeutic results obtained in this series of mainly elderly patients suffering from persistent depressions compares more than favourably with the recorded results of other operative procedures in the same type of case. Freeman (1950) noted that involutional depressions offer a promising field for leucotomy, taking up where convulsion therapy leaves off, and he noted that 60 per cent. of 144 patients had a good result. Pool (1957) finds 85 per cent. of depressive patients improve after brain surgery.

In the present series of 100 patients a 95 per cent. total improvement rate may be regarded as the best one could hope to obtain with any neurosurgical procedure on institutionalized cases, and fully confirms previous reports on the therapeutic efficacy of the Grantham electrocoagulative ventromedial (orbital) leucotomy.

SUMMARY

A study has been made of the therapeutic effects of an orbital leucothermy operation using the Grantham technique and placing an electrolytic lesion in the ventro-medial quadrants of the frontal lobes of 100 patients with persistent depressive psychoses. Assessment of results was made 2 to 7 years after operation, at which time 65 patients were at home, 13 in hospital and 22 dead (3 operative deaths). Most patients were over 50 years old.

The total improvement rate was 96 per cent., 52 patients showing complete recovery. Only one patient showed no clinical improvement, and 87 patients were discharged after operation. There were 12 patients readmitted in temporary relapse. There were no serious post-operative personality defects and only one case of established epilepsy.

An anatomical study was made of the brain of an improved patient dying after 3 months with coronary thrombosis. It is concluded that the Grantham electrocoagulative procedure is an accurate though closed leucotomy technique with a wide range of modification and capable of producing maximal therapeutic results with minimal adverse physical or personality defects. It is particularly suitable for the old and debilitated patients.

ACKNOWLEDGMENTS

I wish to thank Mr. James Hardman, Neurological Surgeon to the United Sheffield Hospitals, for his help and advice upon the preparation of this paper, and also Dr. L. Wolman, for his neuropathological reports, photographs, and valuable suggestions.

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Reviews

Psychopharmaca: A Bibliography of Psychopharmacology 1952-57. By ANNE E. CALDWELL. U.S. Government Printing Office. Washington, 1958. Pp. 258. Price $1.50.

Psychopharmacology is one of the most rapidly developing fields of psychiatry. The literature reporting investigations on the effects of psychotrophic drugs has now reached voluminous proportions and the output continues at an unprecedented rate. A comprehensive bibliography is therefore greatly welcomed.

This bibliography was compiled by the National Library of Medicine of the U.S. Public Health Service at the request of the Psychopharmacology Service Centre of the National Institute of Mental Health, Bethesda, Maryland.

It contains references to approximately 2,500 articles published during the quinquennium extending from January, 1952, to December, 1956, and in addition an incomplete list for 1957. The bibliography is set out as follows:

(1) *A Drug Index* is provided to help in locating entries in the bibliography and gives chemical names, generic names as well as trade names of drugs. It also gives the names of drug groups.

(2) *Subject List of Drugs* which gives names of drugs in alphabetical order. Under each name references are grouped in subdivisions regarding therapeutic use and untoward effects.

(3) Ancillary list of special subjects containing articles referring to Aged patients, Alcoholism, Children, Pain, etc.

(4) Author List arranged alphabetically.

This book is well set out and is both comprehensive and accurate, when tested by a series of checks selected at random. It fills an urgent need and the next bibliography covering 1957 onwards will be eagerly awaited.

W. LINFORD REES.

Aids to Neurology. By E. A. BLAKE PRITCHARD. 2nd Edition. Baillière, Tindall & Cox, London, 1959. Pp. 480.

This is a well-written book containing lucid and concise descriptions of neurological disorders. Its summarized mode of presentation does not detract from its interest, clarity or easy assimilation. The book is commendable for its emphasis on the clinical approach to neurology.

A special chapter is devoted to the anatomical and physiological basis of clinical symptoms together with a scheme for routine examination of the nervous system.

This book should prove invaluable to students and medical practitioners alike.

W. LINFORD REES.

Schizophrenia. A Review of the Syndrome. Ed. by LEOPOLD BELLAK. Logos Press, New York, 1958. Pp. 1010. $14.75.

Nowadays the clinician and the research worker depend more and more on those of their colleagues who undertake the task of surveying critically the work done in various fields of study. Those reviews have become important research tools and much depends on their reliability and precision. Their authors fulfil a function as essential for progress as that of the keeper of a scientific museum. To do this work well requires a special gift of which a critical mind and the collector's enthusiasm are important components. Personal bias is an advantage if it is combined with tolerance for, and a profound interest in, different orientations. The editor of this book meets all those requirements. Together with a team of workers pre-eminent in their respective fields, he has produced a standard work which will remain unsurpassed as a reference book for a considerable time to come. Clinical psychiatrists, epidemiologists, psychoanalysts, psychologists, anthropologists, physiologists and therapists of all orientations will find this book invaluable. Among the contributors are Paul Hoch, Winifred Overholser, Paul Lemkau, Harry Freeman, Milton Greenblatt, Kenneth Appel, Paul Benedict and many other well-known authors. The editor who was the sole author of an earlier study on schizophrenia (1947), was well advised this time to share his labours with experienced colleagues. There is no approach to the problem of schizophrenia which is not represented. The bibliography together with author and subject index fills 253 pages. Over 4,000 contemporary studies have been reviewed. This book does credit to the editor and his associates as well as to the publishers.

E. STENGEL.

Imagination and Thinking: A Psychological Analysis. By PETER MCKELLAR. London, 1957. Pp. 219, Price 21s.

The preoccupation of most contemporary academical psychologists with learning theory and, more recently, with problems of personality, has led to a neglect of the study of thinking. Dr. McKellar is one of the few who has made valuable contributions on various aspects of normal and abnormal thought processes, especially in his studies on the effects of mescaline and of hypnagogic imagery. In this book he presents the results of some of his studies, which he integrates with those of other workers. He distinguishes between "R-thinking", i.e., reality-adjusted thinking, on the one hand and "A-thinking", autism, on the other. The former "characterizes sanity and waking consciousness in their more logical, realistic and prejudice-free moments". By contrast, A-thinking is characteristic of sleep and the hypnagogic state. This division cuts across that between normal and abnormal thinking. The book is concerned with the various manifestations of those two types of thinking, their interactions and disturbances. Of particular interest are the chapters on conditions of creativity, on works of art as thought products and on scientific thinking. This is a most stimulating and thought provoking book which is of particular interest to the psychiatrist.

E. STENGEL.

A Compendium of Research and Theory on Stuttering. By CHARLES F. DIEHL, Ph.D. American Lecture Series. Charles C. Thomas, Springfield, Ill. Pp. 314, Price 73s. 6d.

It has been estimated that there are at least one million stutterers in the United States. This book contains 193 abstracts of articles on stuttering published in English. Each abstract consists of four paragraphs under the headings: purpose, experimental design, summary, conclusions. According to the subject matter, the material has been ordered into five sections, i.e., history, symptomatology, aetiology-physiological, aetiology-psychological, therapy. Each chapter has a bibliography of additional reading references. This compendium presents a new and highly effective method of abstracting selected literature for the use of practitioners and research workers in a specialized field.

E. STENGEL.

The Organic Psychoses. A Guide to Diagnosis. By J. G. DEWAN and W. B. SPAULDING. University of Toronto Press. 1958. Pp. 170.

The authors must have felt that owing to the preoccupation of most psychiatric research workers with the "functional" psychoses and the neuroses, there was a danger of the organic mental disorders being neglected. Medical students and general practitioners will find this book useful. The postgraduate student of psychiatry will find it uneven and insufficiently comprehensive and scholarly for his requirements. It is a primer rather than a monograph. Its unsophisticated practical orientation and easy readability should recommend it to those with little time or no mind for consulting more ambitious texts.

E. STENGEL.

Der Mongolismus. Erscheinungsbild und Herkunft. (Mongolism. Manifestations and Origin). By KARL KÖNIG. Hippokrates-Verlag, Stuttgart. Pp. 278.

The author has for many years been one of the leading authorities in the care and management of mongoloid children and adolescents. He wants his book to be regarded not only as the product of his close study of mongolism, but as the outcome of his personal relationship to his mongol patients, for whom he obviously has a deep affection. He is convinced that mongolism appeared suddenly about a century ago and has spread in our civilization like an epidemic ever since. The book falls into three parts. The first deals with the manifestations and distribution of mongolism. The author agrees with those who regard acute or chronic exhaustion of the mother's reproductive capacity as an important aetiological factor. He believes that male mongols are more frequently born during summer than females, the majority of the latter being born in winter. He views the mongol as a primitive human species rather than the outcome of a maldevelopment, and he regards the recent discovery of the abnormal chromosomal structure as a confirmation of his theory. He attributes the exhaustion of the reproductive capacity to a reversal to the matriarchal hierarchy in the families concerned. Thus mongolism presents primarily a sociological rather than a medical problem. In the final chapter the author presents some valuable observations concerning care, education and treatment of mongols. The book will be read with interest by workers in this special field, even if they should not follow the author's theories, which he presents with commendable modesty.

E. STENGEL.

Behavioral Analysis: Analysis of Clinical Observations of Behavior; as Applied to Mother-Newborn Relationships. By DAVID M. LEVY. Charles C. Thomas, Springfield, Illinois, U.S.A., 1958. Pp. xxxiv+370. Price 72*s*.

The attitude of the mother to her newborn child has been widely regarded as a factor of importance in determining the latter's immediate and perhaps future well-being. There has, however, been little attempt to measure objectively what her attitudes may be, by, for instance, observation of the mother's behaviour. Dr. Levy has long been interested in the subject of maternal attitudes and describes how the present investigation arose out of his study of mothers of patients seen in the practice of child psychiatry. Then, by trial and error, he selected a series of questions to form the basis of a "standardized" enquiry of maternal attitudes. Following from this, the present study, which involves the use of "scores" of maternal attitude was concerned with the observation of mothers and infants in the neonatal period. A trained observer stayed at the foot of the bed and recorded the behaviour of mother and baby, through a feeding or non-feeding time, for 2 or 3 periods, with special reference to the mother's response to the baby, nurse or others. A heterogeneous group of 19 mothers in 4 hospitals was chosen for the purpose. The observation records were then rendered into convenient units representing a numbered series of separate maternal responses and were rated by 4 "judges". Scores were compiled and compared with those obtained from standardized interviews of the mothers; a significant and positive correlation was found between the two. The mother's observed behaviour with her newborn baby could be predicted from an assessment of her maternal interests from questions concerning her past history.

The whole book is devoted to a very detailed description of the methodology used; the analysis of the observations made and a critical appraisal of their validity or otherwise. The readers will need to judge their value for himself. However, as Dr. Levy points out, such methods may be applicable in general to observations of relational behaviour, especially of type relationships of pairs, whether human or animal. He has applied it, for instance, to a study of schizophrenic mothers and their children.

W. WARREN.

Longitudinal Studies of Child Personality: Abstracts with Index. By ALAN A. STONE and GLORIA COCHRANE ONQUÉ. Harvard University Press, 1959. Pp. 314. Price 40*s*.

The authors, while working for the late Dr. Ernst Kris and for Dr. Milton J. E. Senn, of the Yale University Child Study Center, undertook an extensive review of bibliographical references of longitudinal studies in child development and made abstracts of the pertinent articles up to 1955. This work was a preliminary to the publication of further papers and the results of a longitudinal study undertaken at this Center. It was considered that such an annotated bibliography would be valuable to other investigators.

It is of some value, covering 297 articles, mostly from American Journals, of psychological (emotional and social) behaviour in infants and children, wherever a longitudinal approach had been used. It is carefully indexed as regards subject matter, so that the inclusion in addition of an index of authors and of the titles of the articles abstracted would have been worth while.

W. WARREN.

PHENOTHIAZINE DERIVATIVES IN THE TREATMENT OF SCHIZOPHRENIA

By

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INTRODUCTION

THE use of drugs in order to calm excited mental patients dates back to the 5th Century B.C. or earlier.

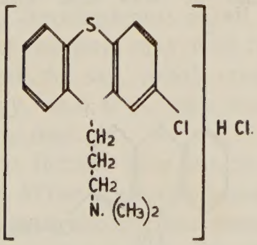
The employment of extracts of the mandrake, Mandragora, in states of motor excitement is attributed to Hippocrates (Belloni, 1957). One disadvantage of such extracts was that reduction of agitation and anxiety could only be achieved at a cost of clouding of consciousness. This is also the case with many modern sedatives.

Extracts of the dried root of *Rauwolfia serpentina* Bentham have been used for centuries by Ayurvedic practitioners in India. Their use was revived recently (Sen and Bose, 1931).

The alkaloids of Rauwolfia reduce agitation and anxiety but produce only minimal clouding of consciousness.

For such drugs the terms "tranquillizers" (from the Latin, *tranquillus*, meaning quiet, calm, still) and "ataractic" drugs (from the Greek, *ἀτάρακτος*, without confusion, cool, steady) have recently been coined.

A number of derivatives of phenothiazine have been found to fulfil these criteria. Systematic study at the Rhône-Poulenc-Spécia Laboratories produced chlorpromazine hydrochloride, a substance resembling promethazine but with a more marked central depressant action:



2-chloro-10-(3-dimethylaminopropyl) phenothiazine hydrochloride.*

This was used with 20 psychiatric patients and gave very favourable results. The trial, however, was uncontrolled (Delay, Deniker and Harl, 1952). Arnold, St. Hift and Solms (1952) obtained good results in an uncontrolled trial with 21 confused or manic patients.

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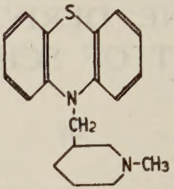
* Largactil (May & Baker), Thorazine (Smith, Kline & French), Megaphen (German workers), Ampliactil (Spanish workers), Aminazine (Russian workers), 4560 RP (Rhône-Poulenc-Spécia), SKF 2601A.

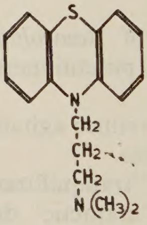
Pecazine



10-(1-methyl-3-piperidylmethyl) phenothiazine*, was not found useful by Kline and Jacob (1955) in a small, uncontrolled group of five patients. However, it was found to benefit a variety of psychiatric syndromes by Hiob and Hippius (1955). The trial was uncontrolled. The authors described the results obtained by combining the drug with chlorpromazine hydrochloride as dumbfounding ("verbluffend").

Werenberg (1955) reported an uncontrolled trial from Denmark, saying that the use of the drug had permitted the abandonment of various means of mechanical restraint.

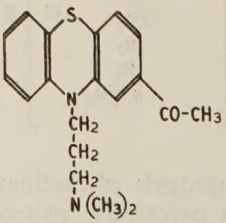
Promazine



10-(3-dimethylaminopropyl)-phenothiazine†, was used by Fazekas, Schultz, Sullivan and Shea (1956) on 407 acutely disturbed patients in an uncontrolled investigation. Good results were reported.

Piperidinochlorphenothiazine‡ was used by Malitz and Hoch (1956) on a small, uncontrolled group of psychiatric patients in doses of 100–1,000 mg. daily. They concluded that it was less effective than chlorpromazine hydrochloride.

Acepromazine



2-acetyl-10-(3-dimethylaminopropyl) phenothiazine§ was used by Delay, Pichot and Ropert (1957) in an uncontrolled investigation of 20 psychotic

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* Pacatal (Warner), Mepazine, Lacumin (Scandinavian workers), P 391, W 1224.

† Sparine (Wyeth), Liranol, RP 3276 (Rhône-Poulenc-Spécia).

‡ NP 207.

§ Notensil (Benger), Plégicil (French workers), 1522 CB, AY-57062.